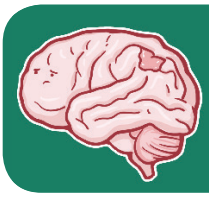

NOTES
AUTONOMIC NERVOUS SYSTEM

- Part of peripheral nervous system (PNS); regulates basic visceral processes necessary to homeostasis
- Autonomic nervous system (ANS) affects visceral organs, glands, involuntary muscles → regulates heart rate, respiration rate, digestion, urination, salivation, sexual arousal, etc.
- Divided into two systems
  - Sympathetic, parasympathetic
- Unlike somatic nervous system, in ANS
  - Neurotransmitters synthesized, stored, released in varicosities (analogous to presynaptic nerve terminals in somatic nervous system)
  - Target organ's tissue can be innervated by multiple postganglionic neurons
  - Postsynaptic receptors widely scattered on target organ

NEURONS

- Two neuron types in both sympathetic, parasympathetic systems
  - Preganglionic, postganglionic
- Preganglionic neurons → preganglionic fibers → synapse with autonomic ganglia (postganglionic neurons) → postganglionic fibers → target organ

Preganglionic neurons

- General visceral efferent (GVE) neurons
- Located in central nervous system (CNS) (spinal cord)
- Release acetylcholine (ACh)

Postganglionic neurons

- GVE, general visceral afferent (GVA) neurons
- Located outside central nervous system
- Release acetylcholine/norepinephrine/neuropeptides

Autonomic ganglia

- Contain neuron cell body clusters (postganglionic neurons)
- Synapse points between preganglionic fibers, postganglionic fibers

SYMPATHETIC NERVOUS SYSTEM

osms.it/sympathetic-nervous-system

- ANS component; controls visceral functions requiring fast response (i.e. "fight or flight")
- Ganglia close to spinal cord → short preganglionic fibers, long postganglionic fibers

Preganglionic neurons

- *Located:* thoracolumbar spinal cord's intermediate horn (T1–L2)
- Cholinergic neurons → release ACh

Postganglionic neurons

- Located close to spinal cord
  - Paravertebral ganglia (cervical, thoracic, rostral lumbar, caudal lumbar, pelvic ganglia)
  - Prevertebral ganglia (celiac, aorticorenal, superior mesenteric, inferior mesenteric ganglion)
  - Chromaffin cells of adrenal medulla (modified sympathetic ganglion)

- Either adrenergic/cholinergic
  - Adrenergic neurons → release norepinephrine/epinephrine (adrenal medulla)
  - Cholinergic → release ACh
- Effector organ receptors: α_1, α_2, β_1, β_2, β_3

Sympathetic nervous system effects

- *Cardiovascular:* ↑ heart rate, ↑ cardiac output, vasoconstriction
- *Respiratory:* bronchodilation
- *Gastrointestinal:* ↓ motility, ↓ secretions
- *Genitourinary:* ↓ bladder's detrusor muscle activity, ejaculation
- *Metabolic:* ↑ gluconeogenesis
- *Glands:* ↓ salivation, ↑ sweating
- *Pupils:* mydriasis

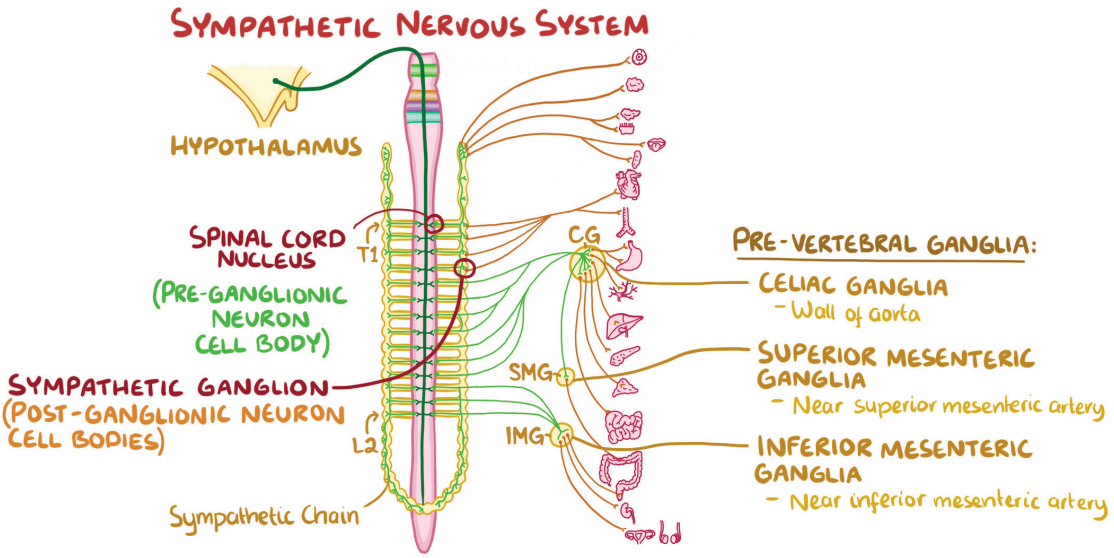

Figure 51.1 Neurons originating in the hypothalamus synapse with sympathetic pre-ganglionic cells bodies in spinal cord nuclei. Some pre-ganglionic neurons synapse in the paravertebral ganglia of the sympathetic chain; others synapse in the pre-vertebral ganglia.

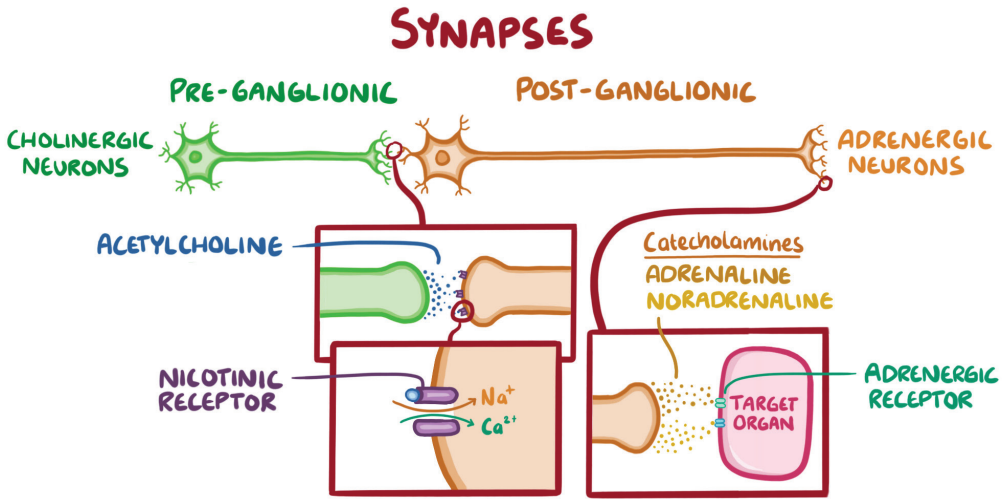

Figure 51.2 Sympathetic preganglionic neurons release acetylcholine, which bind to nicotinic receptors on postganglionic neurons. Postganglionic neurons release catecholamines, which are received by adrenergic receptors on target organs.

PARASYMPATHETIC NERVOUS SYSTEM

osms.it/parasympathetic-nervous-system

- ANS component controls visceral functions not requiring fast response (i.e. "rest and digest")
- Ganglia close to target organ → long preganglionic fibers, short postganglionic fibers

Preganglionic neurons

- Located in brainstem (nuclei of cranial nerves II, VII, IX, X), sacral spinal cord (S2–S4)
- Cholinergic neurons → release ACh

Postganglionic neurons

- Located close to target organs
  - Ciliary ganglion (cranial nerve III)
  - Submandibular ganglion (cranial nerve VII)
  - Otic ganglion (cranial nerve IX)
  - Near/inside target organ (cranial nerve X, sacral nerves)
- Mostly cholinergic, but some non-adrenergic, non-cholinergic → release neuropeptides
- Effector organ receptors are muscarinic

Parasympathetic nervous system effects

- *Cardiovascular:* ↓ heart rate, ↓ cardiac output
- *Respiratory:* bronchoconstriction
- *Gastrointestinal:* ↑ motility, ↑ secretions
- *Genitourinary:* ↑ bladder's detrusor muscle activity, erection
- *Metabolic:* ↓ glycogenesis
- *Glands:* ↑ salivation
- *Pupils:* miosis

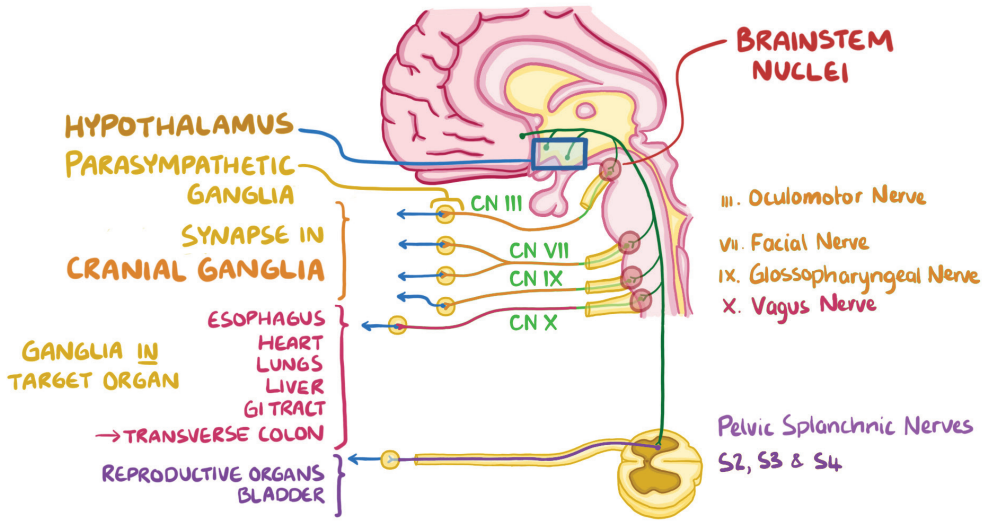

Figure 51.3 Neurons originating in the hypothalamus synapse with parasympathetic pre-ganglionic cells bodies in brainstem, spinal cord at levels S2, S3, and S4. Pre-ganglionic neurons synapse in cranial ganglia and near/in target organ.

NERVE	GANGLIA	LOCATION	INNERVATION
OCULOMOTOR NERVE	CILIARY GANGLIA	BEHIND EYE	PUPIL
FACIAL NERVE	PTERYGOPALATINE GANGLION	PTERYGOPALATINE FOSSA, BEHIND MAXILLA	SUBLINGUAL & SUBMANDIBULAR SALIVARY GLANDS
	SUBMANDIBULAR GANGLION	ABOVE SUBMANDIBULAR SALIVARY GLANDS, in NASAL CAVITY	LACRIMAL GLANDS
			GLANDS in NASAL CAVITY
GLOSSOPHARYNGEAL NERVE	OTIC GANGLIA	INFRATEMPORAL FOSSA, BELOW & MEDIAL TO ZYGOMATIC ARCH	PAROTID SALIVARY GLAND

Figure 51.4 Summary of parasympathetic components of cranial nerves III (oculomotor), VII (facial), and IX (glossopharyngeal).

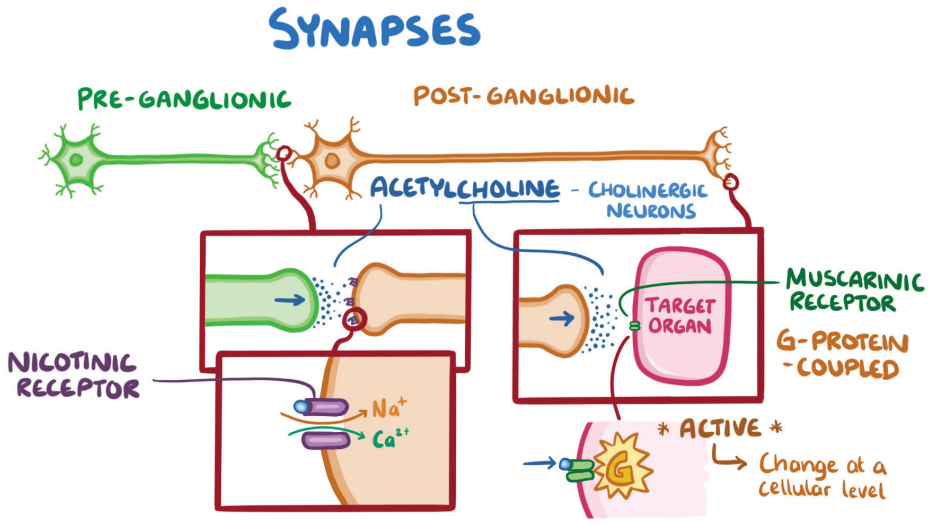

Figure 51.5 Parasympathetic preganglionic neurons release acetylcholine, which binds to nicotinic receptors on the post-ganglionic neuron. The post-ganglionic neuron also releases acetylcholine, which binds to muscarinic (G-protein coupled) receptors on target organs.

SYMPATHETIC & PARASYMPATHETIC NERVOUS SYSTEMS OVERVIEW

	NEURONS	FIBER LENGTH	NEURO-TRANSMITTERS	RECEPTORS
SYMPATHETIC NERVOUS SYSTEM	Preganglionic	Short	ACh	Muscarinic
	Postganglionic	Long	Norepinephrine, ATP, neuropeptide Y	Adrenergic (α_1, α_2, β_1, β_2)
PARASYMPATHETIC NERVOUS SYSTEM	Preganglionic	Long	ACh	Nicotinic (N_n, N_m)
	Postganglionic	Short	ACh	Muscarinic (M_1, M_2, M_3, M_4, M_5)

SYMPATHETIC VS. PARASYMPATHETIC: EFFECTS ON EFFECTORS

	SYMPATHETIC NERVOUS SYSTEM		PARASYMPATHETIC NERVOUS SYSTEM	
EFFECTOR	RECEPTOR	EFFECT	RECEPTOR	EFFECT
PUPILS	α_1	Dilation	M_3	Constriction
HEART	β_1	Positive inotropic, chronotropic, dromotropic effect	M_2	Negative inotropic, chronotropic, dromotropic effect
LUNGS	β_2	Bronchodilation	M_3	Bronchoconstriction, ↑ gland secretion
GI TRACT	α_1	Vasoconstriction, sphincter contraction	M_3	↑ motility, sphincter relaxation, ↑ gland secretion
URINARY TRACT	α_1, β_1	Bladder sphincter contraction, ↑ renin secretion	M_3	Bladder sphincter relaxation
SKELETAL MUSCLE	β_2	Vasodilatation	-	None
SKIN	α_1	Vasoconstriction	-	None
GLANDS	α_1	↑ sweating, ↓ pancreatic activity	M_1, M_3	↑ salivation, ↑ lacrimation, ↑ pancreatic activity

ADRENERGIC RECEPTORS

osms.it/adrenergic-receptors

- *Metabotropic receptors:* respond to catecholamines (norepinephrine, epinephrine)
- Located on sympathetic effector organs → stimulated → sympathetic/sympathomimetic response
- Types
  - *α, β adrenergic receptors:* α_1, α_2, β_1, β_2, β_3

α_1 Adrenergic receptors (stimulatory effect)

- Gastrointestinal tract blood vessels, skin blood vessels → vasoconstriction
- Bladder, gastrointestinal (GI) tract sphincters → contraction
- Radial (dilator) muscle of iris → contraction
- Pancreas → ↓ secretion
- Liver → ↑ glycogenolysis

α_2 Adrenergic receptors (inhibitory effect)

- Presynaptic nerve terminals (autoreceptors) → presynaptic inhibition of neurotransmitter release
- Postganglionic parasympathetic nerve terminals in GI tract (heteroreceptors) → ↓ insulin secretion
- ↓ platelet aggregation

β_1 Adrenergic receptors (stimulatory effect)

- Heart
  - Sinoatrial (SA) node → ↑ heart rate (positive chronotropic effect)
  - Atrioventricular (AV) node → ↑ conduction (positive dromotropic effect)
  - Ventricular muscle → ↑ contractility (positive inotropic effect)
- Salivary glands → ↓ salivation
- Adipose tissue → lipolysis
- Kidney → ↑ renin secretion

β_2 adrenergic receptors (stimulatory effect)

- Skeletal muscle blood vessels → vasodilation
- Bronchioles → relaxation
- Pancreas → ↑ secretion
- Liver → ↑ glycogenolysis, ↑ gluconeogenesis

β_3 adrenergic receptors (stimulatory effects)

- Adipose tissue → lipolysis, thermogenesis
- Detrusor muscle → relaxation

Adrenergic receptor mechanism

- Catecholamines binding → G_q (stimulatory) or G_i (inhibitory) protein activation → second messenger cascade → ↑ phospholipase C or ↓ adenylate cyclase → effect
- α_1 adrenergic receptors
  - G_q protein activation → second messenger cascade → ↑ phospholipase C → ↑ IP_3, DAG, Ca^{2+} → stimulatory effect
- α_2 adrenergic receptors
  - G_i protein activation → ↓ adenylate cyclase → ↓ cAMP → inhibitory effect
- β_1 adrenergic receptors
  - G_s protein activation → ↑ adenylate cyclase → ↑ cAMP → stimulatory effect
- β_1 adrenergic receptors
  - G_s protein activation → ↑ adenylate cyclase → ↑ cAMP → stimulatory effect

CATECHOLAMINES

- Neurotransmitters synthesized, released by adrenergic neurons
- Include epinephrine (adrenaline), norepinephrine (noradrenaline), dopamine

Synthesis

- Tyrosine → L-dopa; catalyzed by tyrosine hydroxylase
- L-dopa → dopamine; catalyzed by dopa decarboxylase
- Dopamine → norepinephrine; catalyzed by β hydroxylase
- Norepinephrine → epinephrine; catalyzed by phenylethanolamine-N-methyltransferase (PNMT); only in adrenal medulla

Degradation

- All catecholamines can be degraded by deamination by monoamine oxidase (MAO)/methylation by catechol-O-methyltransferase (COMT)/both
- Norepinephrine
  - *MAO:* dihydroxymandelic acid
  - *COMT:* normetanephrine
  - *Both:* 3-methoxy-4-hydroxymandelic acid (VMA)
- Epinephrine
  - *MAO:* dihydroxymandelic acid
  - *COMT:* metanephrine
  - *Both:* 3-methoxy-4-hydroxymandelic acid (VMA)
- Dopamine
  - *MAO:* dihydroxyphenylacetic acid
  - *COMT:* 3-methoxytyramine
  - *Both:* homovanillic acid (HVA)

Adrenergic transmission

- Present in
  - Most postganglionic sympathetic neurons (norepinephrine)
  - Adrenal medulla's chromaffin cells (epinephrine)
  - Ventral tegmental area, substantia nigra (dopamine)

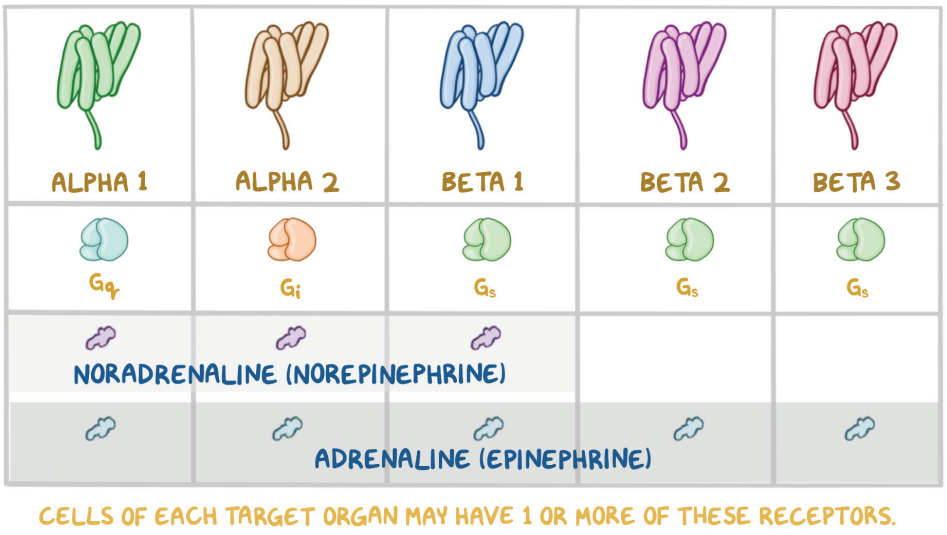

Figure 51.6 Types of adrenergic receptors, the G-proteins with which they can be coupled, and the catecholamines that bind with them.

CHOLINERGIC RECEPTORS

osms.it/cholinergic-receptors

- Receptors respond to neurotransmitter acetylcholine
- Located on parasympathetic effector organs, CNS → stimulated → parasympathetic/parasympathomimetic response

Nicotinic receptors

- Ionotropic receptors
- *Type:* location
  - *Nm:* neuromuscular junction (non autonomic)
  - *Nn:* autonomic ganglia and adrenal medulla
- Mechanism
  - Acetylcholine binding → Na^+, K^+ diffusion → depolarization → voltage Na^+ channel activation → action potential → stimulatory effect

Muscarinic receptors

- Metabotropic receptors (G-protein coupled receptors)
- Located in CNS, all parasympathetic effector organs, some sympathetic effector organs
- *Type:* location
  - M_1: autonomic ganglia, exocrine glands, CNS
  - M_2: heart, sweat glands, CNS
  - M_3: smooth muscle (blood vessels, lungs), glands, eyes, CNS
  - M_4: CNS, sweat glands
  - M_5: CNS
- Mechanism
  - Acetylcholine binding → G_q (stimulatory) or G_i (inhibitory) protein activation → second messenger cascade → ↑ phospholipase C/↓ adenylate cyclase → stimulatory/inhibitory effect
  - M_1, M_3, M_5 → G_q protein activation → ↑ phospholipase C → ↑ IP_3, DAG, Ca^{2+} → stimulatory effect
  - M_4 → G_i protein activation → ↓ adenylate cyclase → ↓ cAMP → inhibitory effect
  - M_2 → G_i protein activation → K^+ channel activation → inhibitory effect

ACETYLCHOLINE (ACh)

- Neurotransmitter synthesized, released by cholinergic neurons
- Synthesis
  - Acetyl CoA + choline → acetylcholine; catalyzed by choline acetyltransferase
- Degradation
  - Acetylcholine → acetylcholine CoA + choline; catalyzed by cholinesterase
- Cholinergic transmission is present in
  - Basal ganglia, hippocampus, cerebral cortex
  - All neuromuscular junctions
  - All preganglionic neurons (both parasympathetic, sympathetic neurons)
  - All postganglionic parasympathetic neurons
  - Some postganglionic sympathetic neurons (sweat glands)

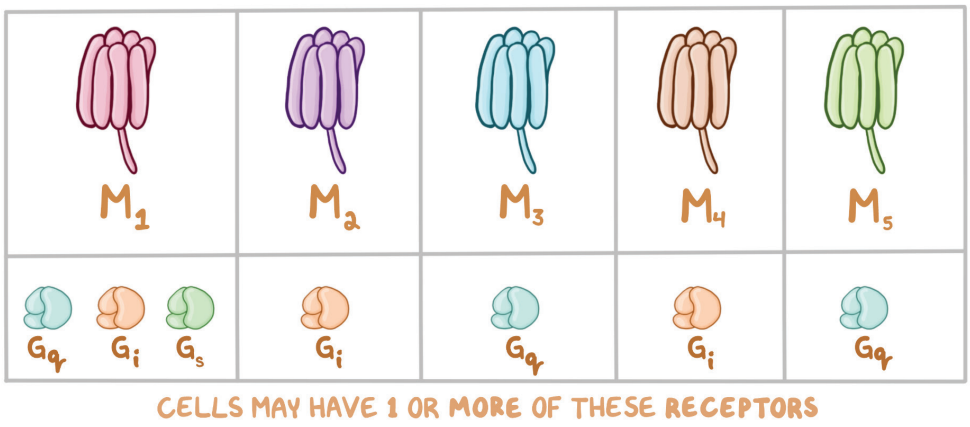

Figure 51.7 Types of muscarinic receptors and the G-proteins with which they can be coupled.

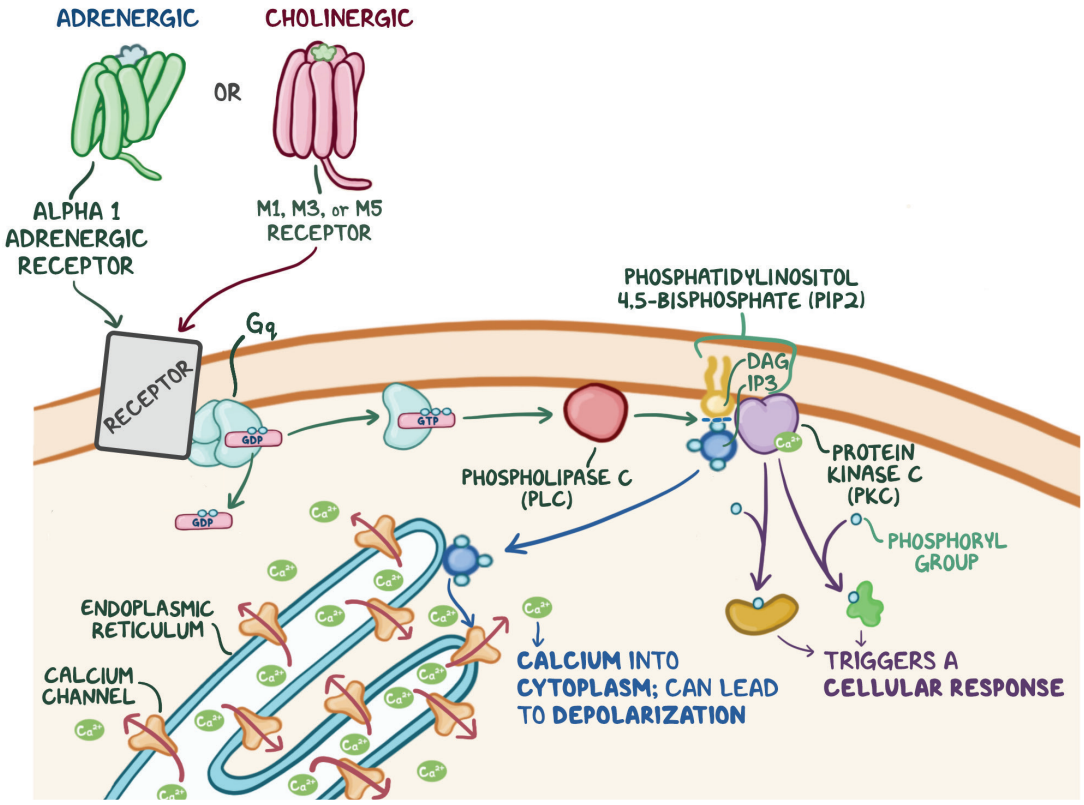

Figure 51.8 Mechanism of action of receptors coupled with G_q protein. The type of adrenergic receptor that couples with G_q protein is the alpha 1 receptor. The types of cholinergic muscarinic receptors that couple with G_q protein are the M_1, M_3, and M_5 receptors.

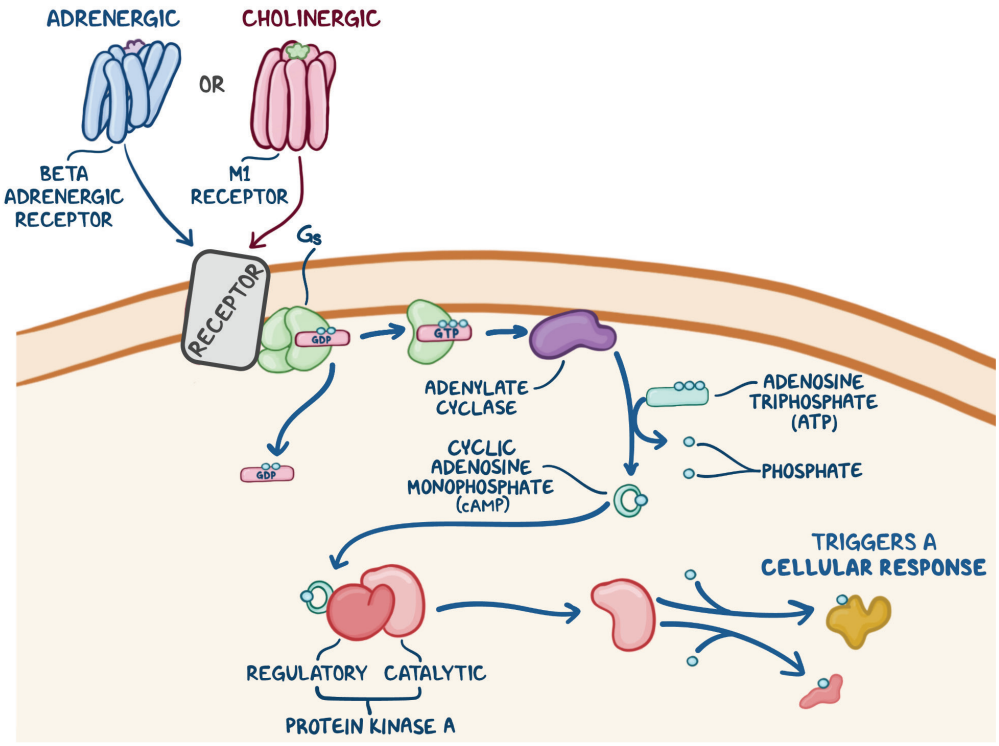

Figure 51.9 Mechanism of action of receptors coupled with G_s protein. The type of adrenergic receptor that couples with G_s protein is the beta receptor. The type of cholinergic muscarinic receptor that couples with G_s protein is the M_3 receptor.

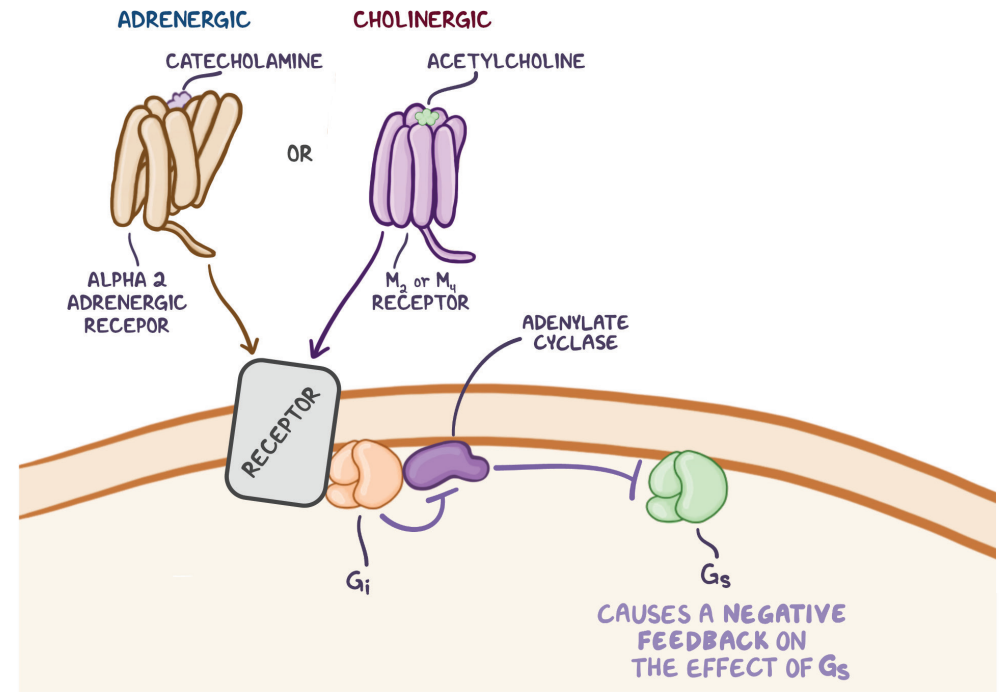

Figure 51.10 Mechanism of action of receptors coupled with G_i protein. The type of adrenergic receptor that couples with G_i protein is the alpha 2 receptor. The types of cholinergic muscarinic receptors that couple with G_i protein are the M_2 and M_4 receptors.