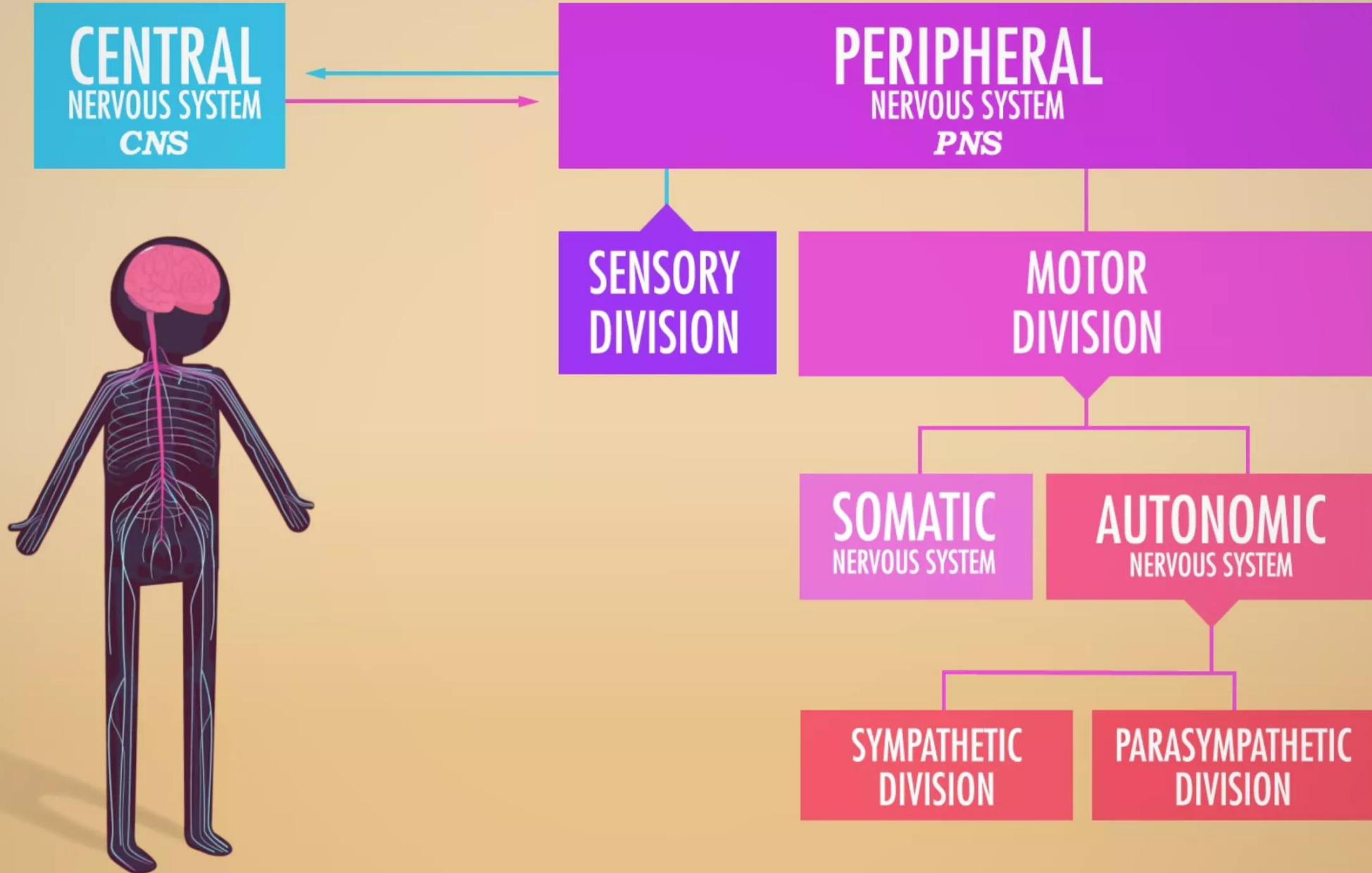# AUTONOMIC NERVOUS SYSTEM

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The Nervous System

INTRODUCTION TO THE NERVOUS SYSTEM

The nervous system is divided into two anatomical divisions: **the central nervous system** (CNS), which is composed of the brain and spinal cord, and the peripheral nervous system, which includes neurons located outside the brain and spinal cord—that is, any nerves that enter or leave the CNS (Figure 3.1).

The peripheral nervous system is subdivided into the **efferent and afferent divisions**. The efferent neurons carry signals away from the brain and spinal cord to the peripheral tissues, and the afferent neurons bring information from the periphery to the CNS.

Afferent neurons provide sensory input to modulate the function of the efferent division through reflex arcs or neural pathways that mediate a reflex action.

Functional divisions within the nervous system

The efferent portion of the peripheral nervous system is further divided into two major functional subdivisions: the somatic and the ANS (Figure 3.1).

The somatic efferent neurons are involved in the **voluntary** control of functions such as contraction of the skeletal muscles essential for locomotion.

The ANS, conversely, regulates the everyday requirements of vital bodily functions **without the conscious** participation of the mind.

It is composed of efferent neurons that innervate smooth muscle of the viscera, cardiac muscle, vasculature, and the exocrine glands, thereby controlling digestion, cardiac output, blood flow, and glandular secretions.
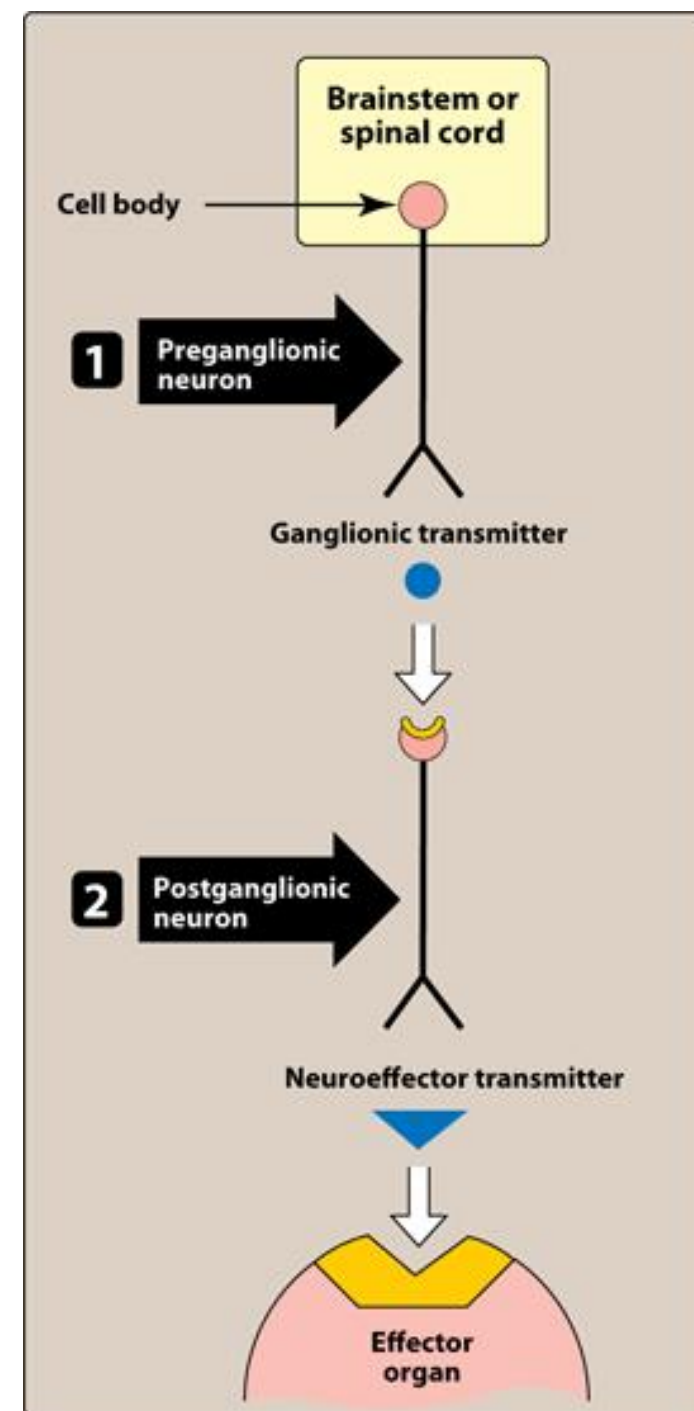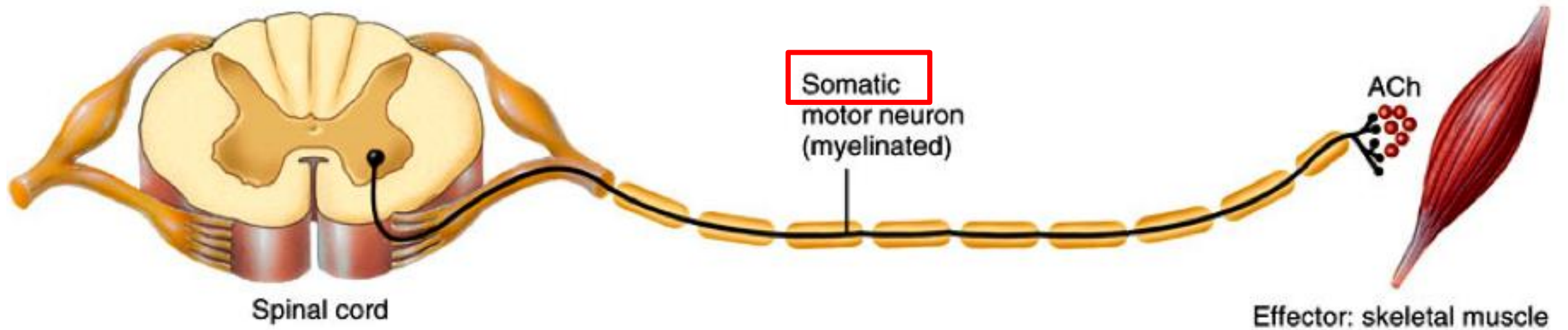
Anatomy of the ANS

1. Efferent neurons: The ANS carries nerve impulses from the CNS to the effector organs by way of two types of efferent neurons: **the preganglionic neurons and the postganglionic neurons.**

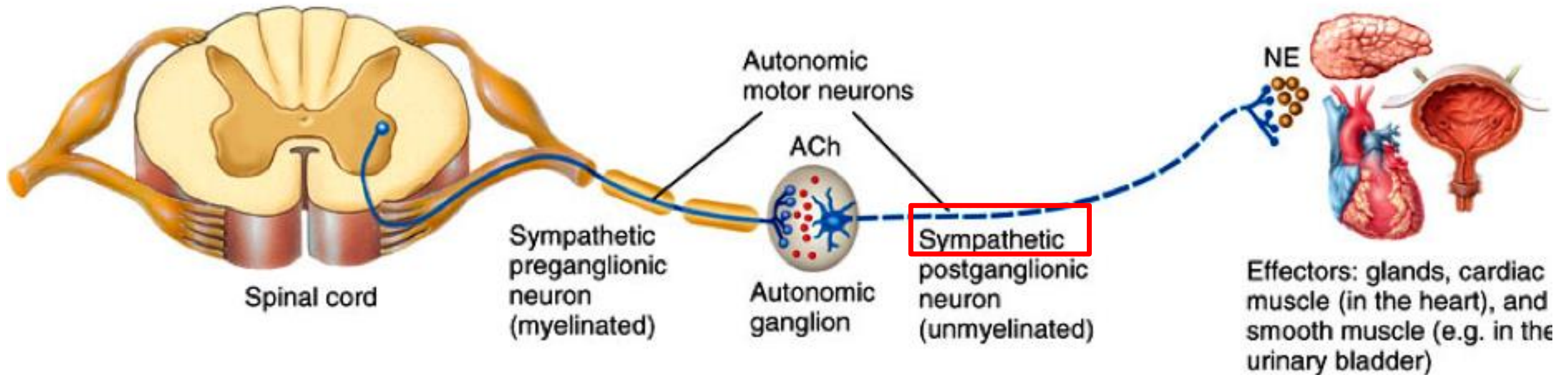The cell body of the first nerve cell, the preganglionic neuron, is located within the CNS.

The preganglionic neurons emerge from the brainstem or spinal cord and make a synaptic connection in ganglia (an aggregation of nerve cell bodies located in the peripheral nervous system).

The ganglia function as relay stations between the preganglionic neuron and the second nerve cell, the postganglionic neuron.

Somatic
motor neuron
(myelinated)

ACh

Spinal cord

Effector: skeletal muscle

(a) Somatic nervous system

Autonomic
motor neurons

ACh

NE

Spinal cord

Sympathetic
preganglionic
neuron
(myelinated)

Autonomic
ganglion

Sympathetic
postganglionic
neuron
(unmyelinated)

Effectors: glands, cardiac
muscle (in the heart), and
smooth muscle (e.g. in the
urinary bladder)

Adrenal cortex

Adrenal medulla

Chromaffin cell

ACh

Sympathetic preganglionic neuron (myelinated)

Adrenal medulla

Spinal cord

Epinephrine and NE

Blood vessel

ACh

Parasympathetic preganglionic neuron (myelinated)

Autonomic ganglion

Parasympathetic postganglionic neuron (unmyelinated)

Spinal cord

Effectors: glands, cardiac muscle (in the heart), and smooth muscle (e.g. in the urinary bladder)

Anatomy of the ANS

2. Afferent neurons: The afferent neurons (fibers) of the ANS are important in the reflex regulation of this system (for example, by sensing pressure in the carotid sinus and aortic arch) and in signaling the CNS to influence the efferent branch of the system to respond.

Anatomy of the ANS

3. Sympathetic neurons: The efferent ANS is divided into the sympathetic and the parasympathetic nervous systems, as well as the enteric nervous system (Figure 3.1).

Anatomically, the sympathetic and the parasympathetic neurons originate in the CNS and emerge from two different spinal cord regions.

The preganglionic neurons of the sympathetic system come from the thoracic and lumbar regions (T1 to L2) of the spinal cord, and they synapse in two cord-like chains of ganglia that run close to and in parallel on each side of the spinal cord.

The preganglionic neurons are short in comparison to the postganglionic ones. Axons of the postganglionic neuron extend from these ganglia to the tissues that they innervate and regulate (see Chapter 6).

Anatomy of the ANS

3. Sympathetic neurons: In most cases, the preganglionic nerve endings of the sympathetic nervous system are highly branched, enabling one preganglionic neuron to interact with many postganglionic neurons.

This arrangement enables this division to activate numerous effector organs at the same time.

The adrenal medulla, like the sympathetic ganglia, receives preganglionic fibers from the sympathetic system. The adrenal medulla, in response to stimulation by the ganglionic neurotransmitter acetylcholine, secretes epinephrine (adrenaline), and lesser amounts of norepinephrine, directly into the blood.

Anatomy of the ANS

4. Parasympathetic neurons: The parasympathetic preganglionic fibers arise from cranial nerves III (oculomotor), VII (facial), IX (glossopharyngeal), and X (vagus), as well as from the sacral region (S2 to S4) of the spinal cord and synapse in ganglia near or on the effector organs.

[Note: The vagus nerve accounts for 90% of preganglionic parasympathetic fibers in the body. Postganglionic neurons from this nerve innervate most of the organs in the thoracic and abdominal cavity.]

Thus, in contrast to the sympathetic system, the preganglionic fibers are long, and the postganglionic ones are short, with the ganglia close to or within the organ innervated.

In most instances, there is a one-to-one connection between the preganglionic and postganglionic neurons, enabling discrete response of this system.

Anatomy of the ANS

5. Enteric neurons: The enteric nervous system is the third division of the ANS. It is a collection of nerve fibers that innervate the gastrointestinal (GI) tract, pancreas, and gallbladder, and it constitutes the "brain of the gut."

This system functions independently of the CNS and controls the motility, exocrine and endocrine secretions, and microcirculation of the GI tract.

It is modulated by both the sympathetic and parasympathetic nervous systems.

Red = Sympathetic actions
Blue = Parasympathetic actions

LACRIMAL GLANDS
Stimulation of tears

EYE
Contraction of iris radial muscle (pupil dilates)

Contraction of iris sphincter muscle (pupil contracts)
Contraction of ciliary muscle (lens accommodates for near vision)

SALIVARY GLANDS
Thick, viscous secretion
Copious, watery secretion

TRACHEA AND BRONCHIOLES
Dilation
Constriction, increased secretions

HEART
Increased rate; increased contractility
Decreased rate; decreased contractility

ADRENAL MEDULLA
Secretion of epinephrine and norepinephrine

KIDNEY
Secretion of renin (β_1 increases; α_1 decreases)

GASTROINTESTINAL SYSTEM
Decreased muscle motility and tone; contraction of sphincters
Increased muscle motility and tone

URETERS AND BLADDER
Relaxation of detrusor; contraction of trigone and sphincter

Contraction of detrusor; relaxation of trigone and sphincter

GENITALIA (female)
Relaxation of uterus

BLOOD VESSELS
(skeletal muscle)
Dilation

GENITALIA (male)
Stimulation of ejaculation
Stimulation of erection

BLOOD VESSELS
(skin, mucous membranes, and splanchnic area)
Constriction
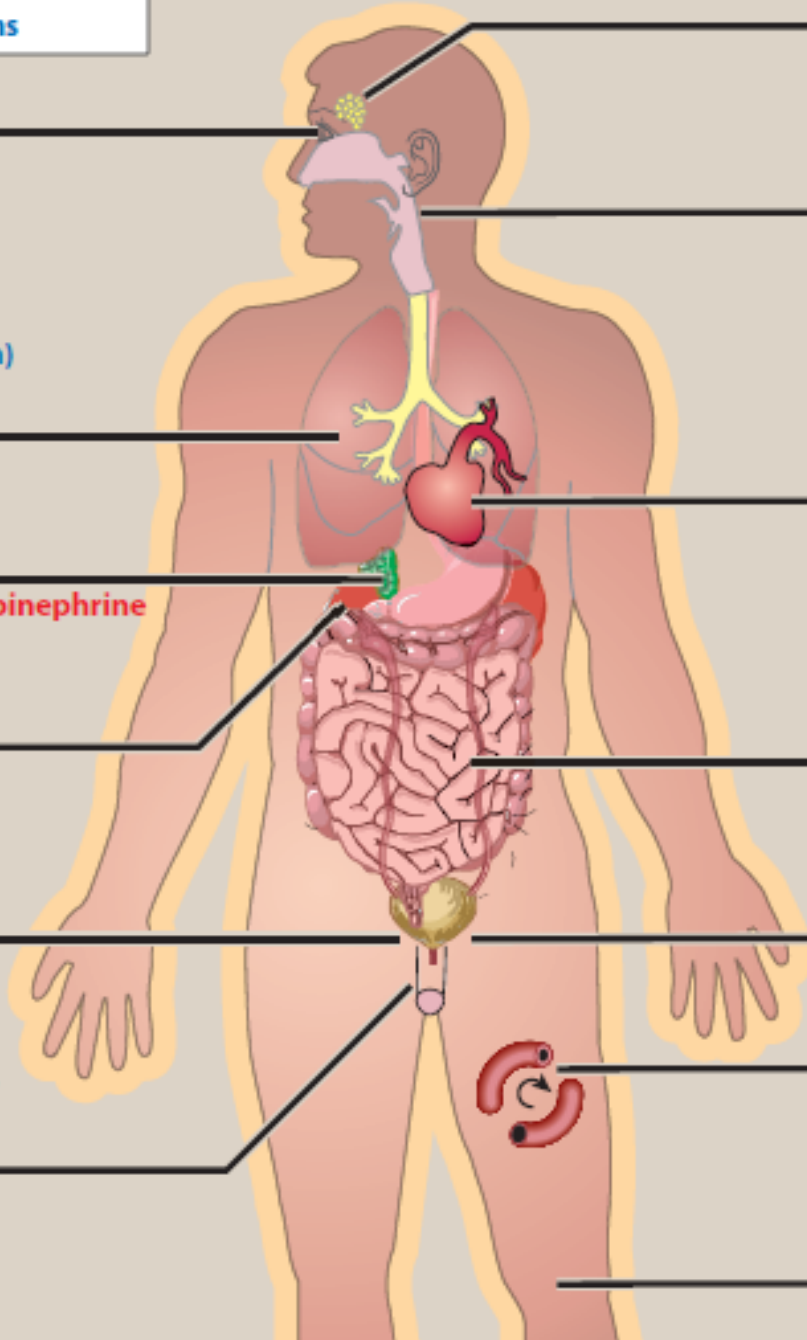
Functions of the sympathetic nervous system

Although continually active to some degree (for example, in maintaining the tone of vascular beds), the sympathetic division has the property of adjusting in response to stressful situations, such as trauma, fear, hypoglycemia, cold, and exercise.

1. Effects of stimulation of the sympathetic division: The effect of sympathetic output is to increase heart rate and blood pressure, to mobilize energy stores of the body, and to increase blood flow to skeletal muscles and the heart while diverting flow from the skin and internal organs.

Sympathetic stimulation results in dilation of the pupils and the bronchioles (Figure 3.3). It also affects GI motility and the function of the bladder and sexual organs.

Functions of the sympathetic nervous system

2. Fight-or-flight response: The changes experienced by the body during emergencies are referred to as the "fight or flight" response (Figure 3.4).

These reactions are triggered both by direct sympathetic activation of the effector organs and by stimulation of the adrenal medulla to release epinephrine and lesser amounts of norepinephrine.

Hormones released by the adrenal medulla directly enter the bloodstream and promote responses in effector organs that contain adrenergic receptors (see Chapter 6).

The sympathetic nervous system tends to function as a unit and often discharges as a complete system, for example, during severe exercise or in reactions to fear.

Functions of the parasympathetic nervous system

The parasympathetic division is involved with maintaining homeostasis within the body.

It is required for life, since it maintains essential bodily functions, such as digestion and elimination of wastes.

The parasympathetic division usually acts to oppose or balance the actions of the sympathetic division and generally predominates the sympathetic system in "rest-and-digest" situations.

Unlike the sympathetic system, the parasympathetic system never discharges as a complete system.

If it did, it would produce massive, undesirable, and unpleasant symptoms, such as involuntary urination and defecation.

Instead, parasympathetic fibers innervating specific organs such as the gut, heart, or eye are activated separately, and the system functions to affect these organs individually.

Role of the CNS in the control of autonomic functions

Although the ANS is a motor system, it does require sensory input from peripheral structures to provide information on the current state of the body.

This feedback is provided by streams of afferent impulses, originating in the viscera and other autonomically innervated Structures that travel to integrating centers in the CNS, such as the hypothalamus, medulla oblongata, and spinal cord.

These centers respond to the stimuli by sending out efferent reflex impulses via the ANS.
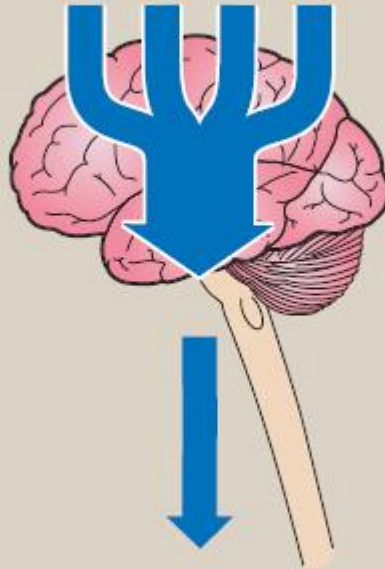
Role of the CNS in the control of autonomic functions

"Fight-or-flight" stimulus

Sympathetic output
(diffuse because postganglionic neurons may innervate more than one organ)

"Rest-and-digest" stimulus

Parasympathetic output
(discrete because postganglionic neurons are not branched, but are directed to a specific organ)

Sympathetic and para-sympathetic actions often oppose each other

Role of the CNS in the control of autonomic functions

1. Reflex arcs: Most of the afferent impulses are involuntarily translated into reflex responses.

For example, a fall in blood pressure causes pressure-sensitive neurons (baroreceptors in the heart, vena cava, aortic arch, and carotid sinuses) to send fewer impulses to cardiovascular centers in the brain.

This prompts a reflex response of increased sympathetic output to the heart and vasculature and decreased parasympathetic output to the heart, which results in a compensatory rise in blood pressure and tachycardia.

[Note: In each case, the reflex arcs of the ANS comprise a sensory (or afferent) arm and a motor (or efferent or effector) arm.]

2. Emotions and the ANS: Stimuli that evoke strong feelings, such as rage, fear, and pleasure, can modify the activities of the ANS.

Innervation by the ANS

1. Dual innervation: Most organs in the body are innervated by both divisions of the ANS. Thus, vagal parasympathetic innervation slows the heart rate, and sympathetic innervation increases the
heart rate.

Despite this dual innervation, one system usually predominates in controlling the activity of a given organ. For example, in the heart, the vagus nerve is the predominant factor for controlling rate.

This type of antagonism is considered to be dynamic and is fine tuned continually to control homeostatic organ functions.

2. Organs receiving only sympathetic innervation: Although most tissues receive dual innervation, some effector organs, such as the adrenal medulla, kidney, pilomotor muscles, and sweat glands, receive innervation only from the sympathetic system.

Somatic nervous system

The efferent somatic nervous system differs from the ANS in that a single myelinated motor neuron, originating in the CNS, travels directly to skeletal muscle without the mediation of ganglia.

As noted earlier, the somatic nervous system is under voluntary control, whereas the ANS is involuntary. Responses in the somatic division are generally faster than those in the ANS.

CHEMICAL SIGNALING BETWEEN CELLS

Neurotransmission in the ANS is an example of the more general process of chemical signaling between cells.

In addition to neurotransmission, other types of chemical signaling include the secretion of hormones and the release of local mediators

CHEMICAL SIGNALING BETWEEN CELLS

A. Hormones

Specialized endocrine cells secrete hormones into the bloodstream, where they travel throughout the body, exerting effects on broadly distributed target cells.

B. Local mediators

Most cells in the body secrete chemicals that act locally on cells in the immediate environment. Because these chemical signals are rapidly destroyed or removed, they do not enter the blood and are not distributed throughout the body. Histamine (see Chapter 30) and the prostaglandins are examples of local mediators.

C. Neurotransmitters

Communication between nerve cells, and between nerve cells and effector organs, occurs through the release of specific chemical signals (neurotransmitters) from the nerve terminals.

CHEMICAL SIGNALING BETWEEN CELLS

C. Neurotransmitters … Cont.

This release is triggered by the arrival of the action potential at the nerve ending, leading to depolarization.

An increase in intracellular Ca2+ initiates fusion of the synaptic vesicles with the presynaptic membrane and release of their contents.

The neurotransmitters rapidly diffuse across the synaptic cleft, or space (synapse), between neurons and combine with specific receptors on the postsynaptic (target) cell.

CHEMICAL SIGNALING BETWEEN CELLS

1. Membrane receptors: All neurotransmitters, and most hormones and local mediators, are too hydrophilic to penetrate the lipid bilayers of target cell plasma membranes.

Instead, their signal is mediated by binding to specific receptors on the cell surface of target organs.
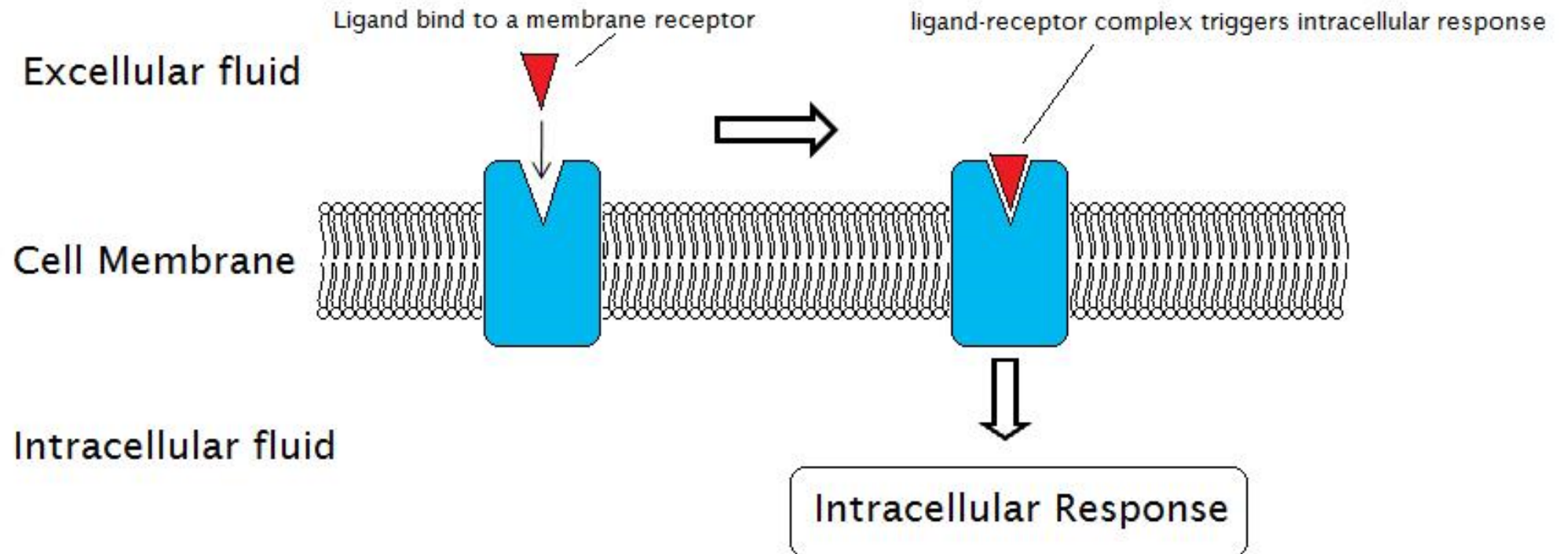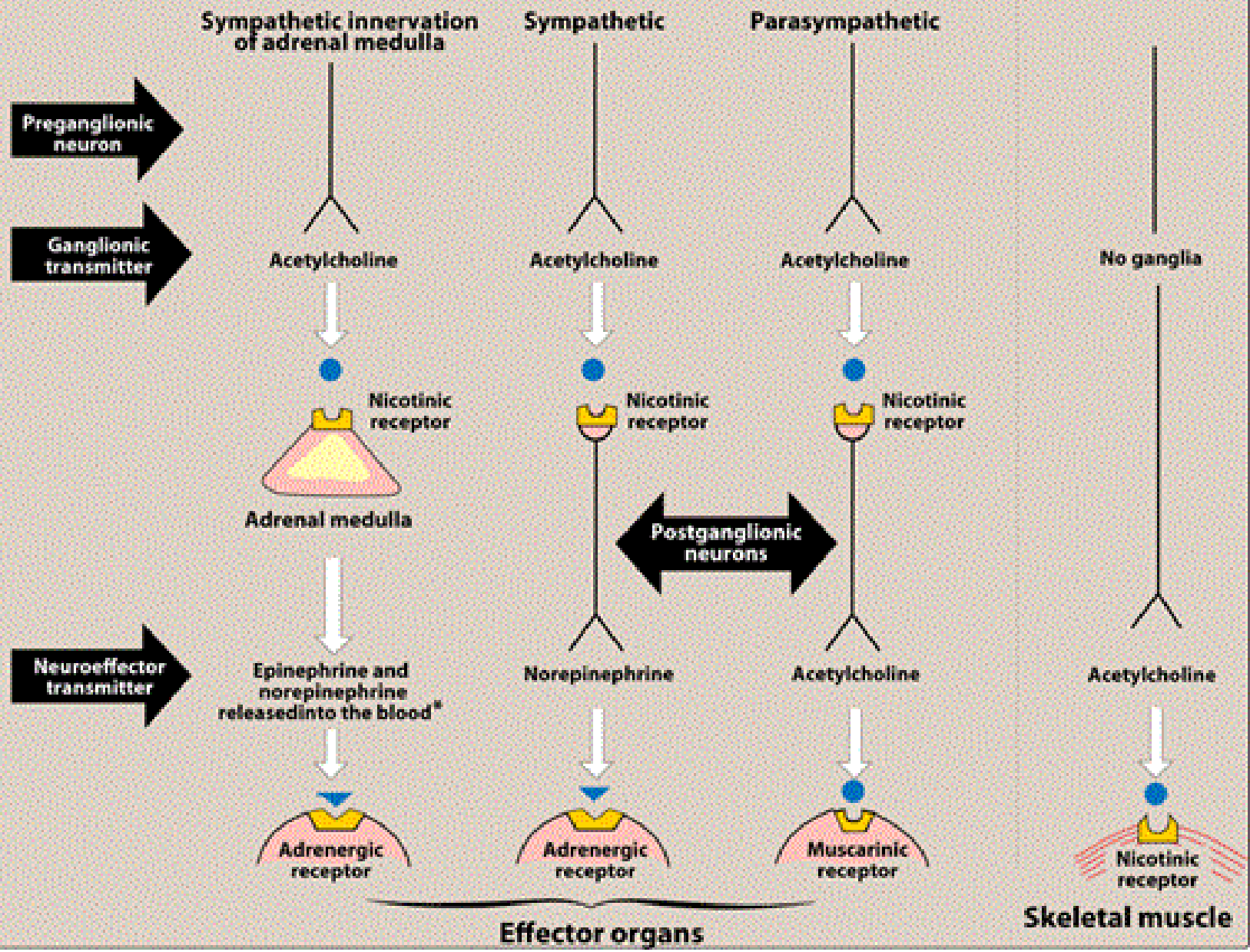
2. Types of neurotransmitters:

Although over 50 signal molecules in the nervous system have been identified, **norepinephrine (and the closely related epinephrine), acetylcholine, dopamine, serotonin, histamine, glutamate, and γ-aminobutyric acid** are most commonly involved in the actions of therapeutically useful drugs.

Each of these chemical signals binds to a specific family of receptors.

Acetylcholine and norepinephrine are the primary chemical signals in the **ANS**, whereas a wide variety of neurotransmitters function in the CNS.

2. Types of neurotransmitters: a. Acetylcholine:

The autonomic nerve fibers can be divided into two groups based on the type of neurotransmitter released. If transmission is mediated by acetylcholine, the neuron is termed cholinergic.

Acetylcholine mediates the transmission of nerve impulses across autonomic ganglia in both the sympathetic and parasympathetic nervous systems. It is the neurotransmitter at the adrenal medulla.

Transmission from the autonomic postganglionic nerves to the effector organs in the parasympathetic system, and a few sympathetic system organs, also involves the release of acetylcholine.

In the somatic nervous system, transmission at the neuromuscular junction (the junction of nerve fibers and voluntary muscles) is also cholinergic.
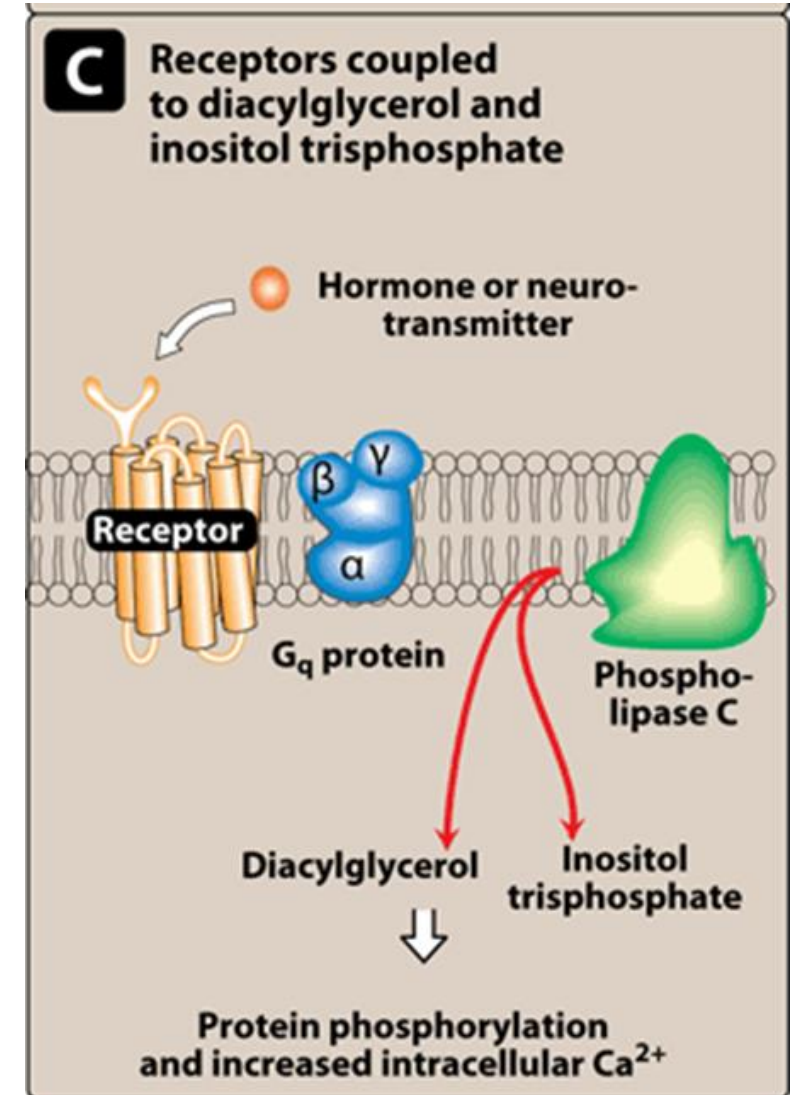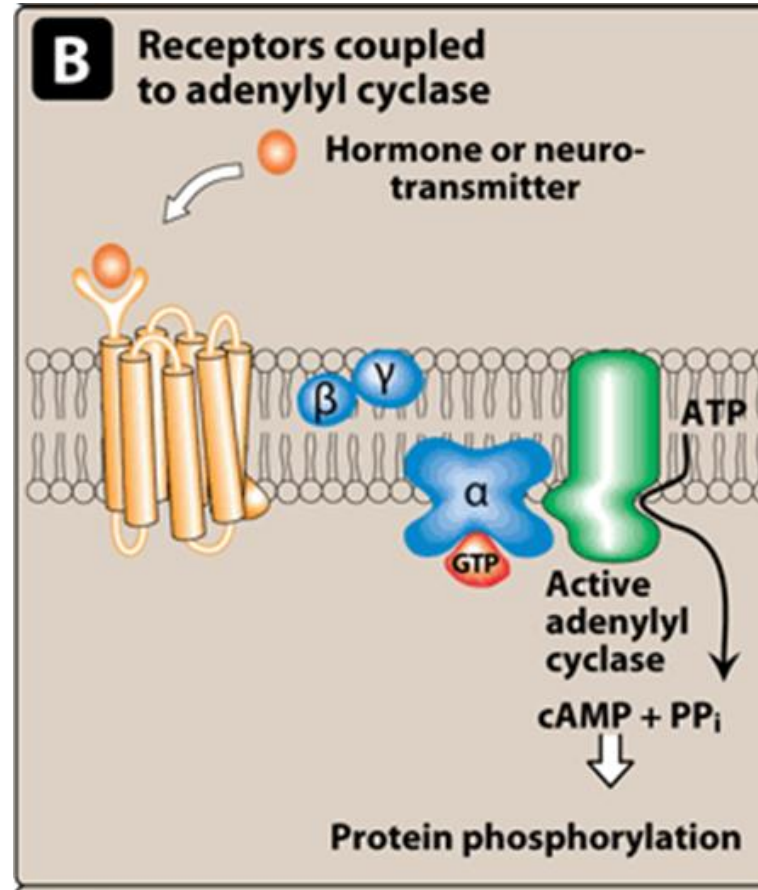
2. Types of neurotransmitters: b. Norepinephrine and epinephrine:

When norepinephrine and epinephrine are the neurotransmitters, the fiber is termed adrenergic.

In the sympathetic system, norepinephrine mediates the transmission of nerve impulses from autonomic postganglionic nerves to effector organs.

[Note: A few sympathetic fibers, such as those involved in sweating, are cholinergic, and, for simplicity, they are not shown in Figure 3.8.]

SIGNAL TRANSDUCTION IN THE EFFECTOR CELL

A Receptors coupled to ion channels

Neuro-transmitter

Cl^-

Extra-cellular space

Cell membrane

Cell membrane

Cytosol

Cl^-

Changes in membrane potential or ionic concentration within cell

B Receptors coupled to adenylyl cyclase

Hormone or neuro-transmitter

β γ

α

GTP

ATP

Active adenylyl cyclase

cAMP + PP$_i$

Protein phosphorylation

C Receptors coupled to diacylglycerol and inositol trisphosphate

Hormone or neuro-transmitter

Receptor

β γ

α

G_q protein

Phospho-lipase C

Diacylglycerol

Inositol trisphosphate

Protein phosphorylation and increased intracellular Ca^{2+}

Three mechanisms whereby binding of a neurotransmitter leads to a cellular effect

SIGNAL TRANSDUCTION IN THE EFFECTOR CELL

The binding of chemical signals to receptors activates enzymatic processes within the cell membrane that ultimately results in a cellular response, such as the phosphorylation of intracellular proteins or changes in the conductivity of ion channels.

A neurotransmitter can be thought of as a signal and a receptor as a signal detector and transducer.

Second messenger molecules produced in response to a neurotransmitter binding to a receptor translate the extracellular signal into a response that may be further propagated or amplified within the cell.

Each component serves as a link in the communication between extracellular events and chemical changes within the cell (see Chapter 2).

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A. Membrane receptors affecting ion permeability (ionotropic receptors)

Neurotransmitter receptors are membrane proteins that provide a binding site that recognizes and responds to neurotransmitter molecules.

Some receptors, such as the postsynaptic nicotinic receptors in the skeletal muscle cells, are directly linked to membrane ion channels.

Therefore, binding of the neurotransmitter occurs rapidly (within fractions of a millisecond) and directly affects **ion permeability** (Figure 3.9A).

These types of receptors are known as **ionotropic receptors.**

B. Membrane receptors coupled to second messengers (metabotropic receptors)

Many receptors are not directly coupled to ion channels. Rather, the receptor signals its recognition of a bound neurotransmitter by initiating a series of reactions that ultimately result in a specific intracellular response.

Second messenger molecules, so named because they intervene between the original message (the neurotransmitter or hormone) and the ultimate effect on the cell, are part of the cascade of events that translate neurotransmitter binding into a cellular response, usually through the intervention of a G protein.

The two most widely recognized second messengers are the adenylyl cyclase system and the calcium/phosphatidylinositol system (Figure 3.9B, C).

The receptors coupled to the second messenger system are known as **metabotropic receptors**.

Muscarinic and adrenergic receptors are examples of metabotropic receptors.

Summary of differences between sympathetic, parasympathetic, and motor nerves

Major differences in the anatomical arrangement of neurons lead to variations of the functions in each division (Figure 3.6).

The sympathetic nervous system is widely distributed, innervating practically all effector systems in the body.

In contrast, the distribution of the parasympathetic division is more limited. The sympathetic preganglionic fibers have a much broader influence than the parasympathetic fibers and synapse with a larger number of postganglionic fibers.

This type of organization permits a diffuse discharge of the sympathetic nervous system. The parasympathetic division is more circumscribed, with mostly one-to-one interactions, and the ganglia are also close to, or within, organs they innervate.

This limits the amount of branching that can be done by this division.

Summary of differences between sympathetic, parasympathetic, and motor nerves

[A notable exception to this arrangement is found in the myenteric plexus, where one preganglionic neuron has been shown to interact with 8000 or more postganglionic fibers.]

The anatomical arrangement of the parasympathetic system results in the distinct functions of this division.

The somatic nervous system innervates skeletal muscles. One somatic motor neuron axon is highly branched, and each branch innervates a single muscle fiber.

Thus, one somatic motor neuron may innervate 100 muscle fibers.

This arrangement leads to the formation of a motor unit. The lack of ganglia and the myelination of the motor nerves enable a fast response by the somatic nervous system.

1 AFFERENT INFORMATION

Sensory input from the viscera:
- Drop in blood pressure
- Reduced stretch of baroreceptors in aortic arch
- Reduced frequency of afferent impulses to medulla (brainstem)
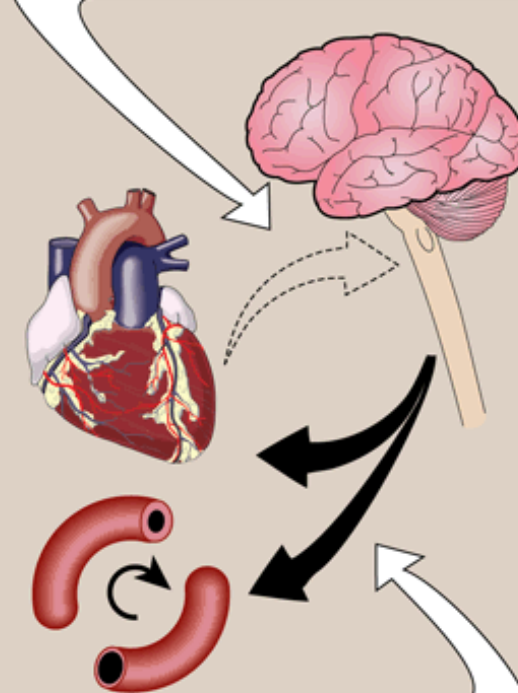
2 REFLEX RESPONSE

Efferent reflex impulses via the autonomic nervous system cause:
- Inhibition of parasympathetic and activation of sympathetic divisions
- Increased peripheral resistance and cardiac output
- Increased blood pressure

Summary of differences between sympathetic, parasympathetic, and motor nerves

	SYMPATHETIC	PARASYMPATHETIC
Sites of origin	Thoracic and lumbar region of the spinal cord (thoracolumbar)	Brain and sacral area of the spinal cord (craniosacral)
Length of fibers	Short preganglionic Long postganglionic	Long preganglionic Short postganglionic
Location of ganglia	Close to the spinal cord	Within or near effector organs
Preganglionic fiber branching	Extensive	Minimal
Distribution	Wide	Limited
Type of response	Diffuse	Discrete