Chapter 13 – Autonomic Nervous System

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by writing short essays, drawing diagrams, and responding to multiple choices or matching questions, at the level of 85% or greater proficiency for each student.

A. To compare and contrast the general neural organization of the somatic motor and autonomic motor systems.
B. To explain the organization and function of the parasympathetic nervous system, including brainstem and spinal neurons, ganglia and ganglionic neurons, neurotransmitters and receptors involved.
C. To describe representative motor actions of the parasympathetic nervous system on the organs.
D. To name representative drugs acting on the parasympathetic nervous system and to explain their actions.
E. To explain the organization and function of the sympathetic nervous system, including the brainstem and spinal neurons, ganglia and ganglionic neurons, neurotransmitters and receptors involved.
F. To describe representative motor actions of the sympathetic nervous system on the organs.
G. To name representative drugs acting on the sympathetic nervous system and to explain their actions.

Somatic vs. Autonomic Motor Organization

The motor neurons that control the skeletal muscles, as described in chapter 12, make up what is often called the **somatic nervous system.** In contrast the motor neurons that control cardiac muscle, smooth muscle, and glands make up what is often called the **autonomic nervous system**. Figure 13.1 compares and contrasts the organization of the somatic motor neurons and the autonomic motor neurons.

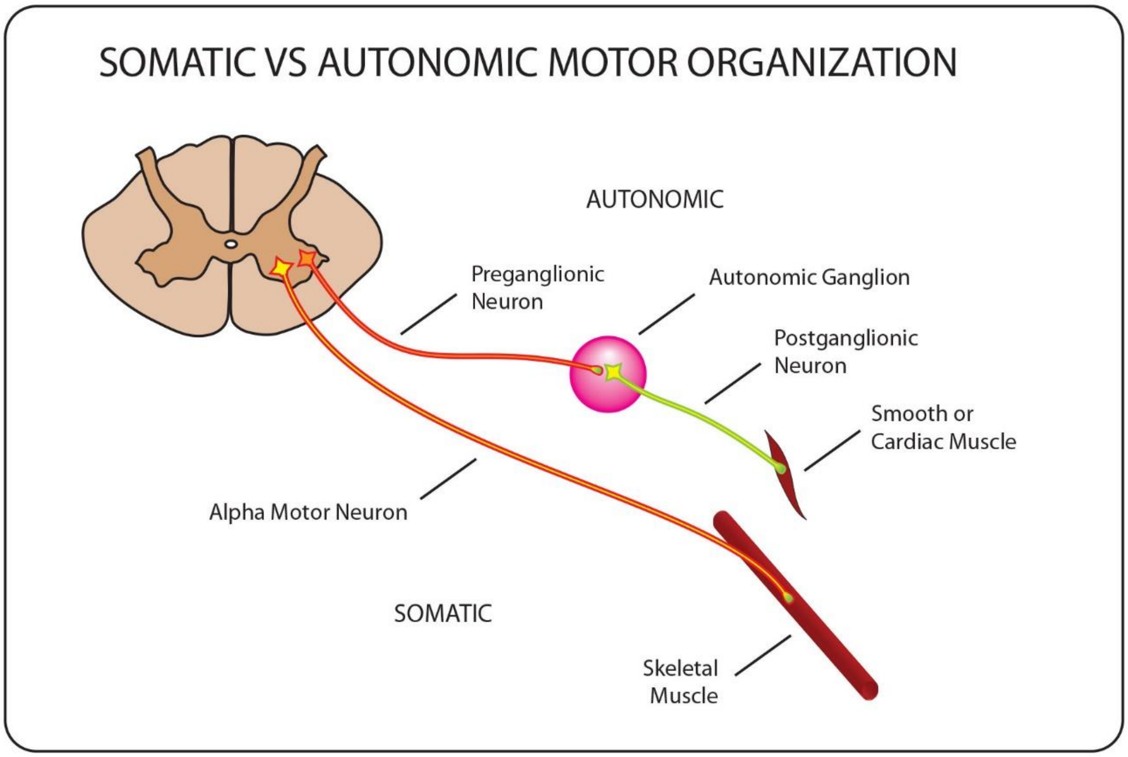

Figure 13.1 © 2014 David G. Ward, Ph.D.

- In the somatic nervous system one motor neuron (an alpha motor neuron) is involved in the connection between the central nervous system and the target organ (the skeletal muscle)
- In the autonomic nervous system two motor neurons are involved in the connection between the central nervous system and the target tissues
    - The first motor neurons are called **preganglionic neurons,** their cell bodies are located within the central nervous system, and their axons synapse on neurons in **autonomic ganglia**.
    - The second motor neurons are called **ganglionic** or **postganglionic neurons,** their cell bodies are located in autonomic ganglia outside of the CNS, and their axons leave the autonomic ganglia to synapse on target tissues.

The autonomic nervous system is composed of two divisions; the **parasympathetic** division and the **sympathetic** division. These two divisions generally have opposing actions on the target tissues.

Parasympathetic Division

Brainstem and Sacral Spinal organization

The cell bodies of parasympathetic preganglionic neurons (the first motor neurons in line) originate either from nuclei of the brainstem or from the lateral horns of the sacral spinal cord, as shown in Figure 13.2. The axons of the preganglionic neurons travel either through cranial nerves or through sacral spinal nerves.

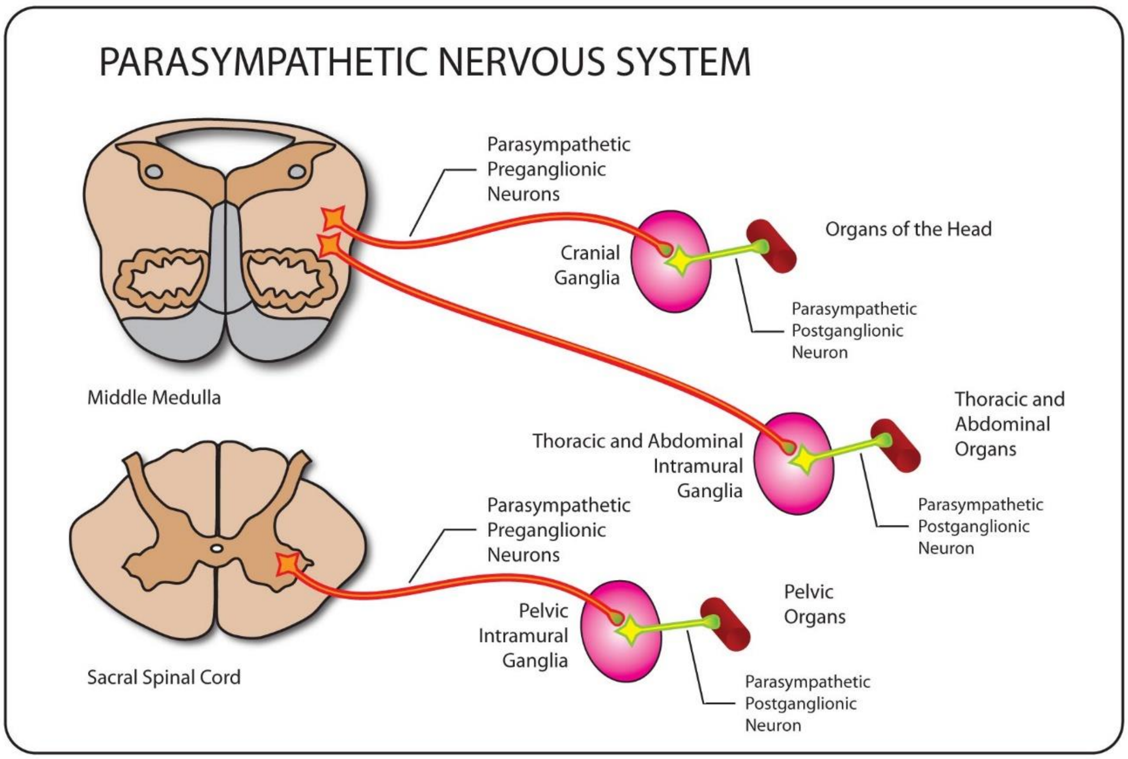

Figure 13.2 © 2014 David G. Ward, Ph.D.

- Preganglionic axons targeting the head travel through the III, VII, and IX cranial nerves and synapse on ganglionic neurons in the cranial ganglia, which in turn travel to the target tissues in the head.
- Preganglionic axons targeting thoracic and abdominal organs travel through the X cranial nerve and synapse on ganglionic neurons in the thoracic and abdominal intramural ganglia, which in turn travel to the target tissues in these organs.
- Preganglionic axons targeting pelvic organs travel through sacral spinal nerves and synapse on ganglionic neurons in the pelvic intramural ganglia, which in turn travel to the target tissues in the pelvis.

Neurotransmitters

The actions of parasympathetic preganglionic neurons and of the parasympathetic postganglionic neurons depend on the neurotransmitters and receptors involved. The organization of the parasympathetic neurotransmitters is shown in Figure 13.3. The mechanisms of action of nicotinic and muscarinic receptors are summarized in Table 13.1.

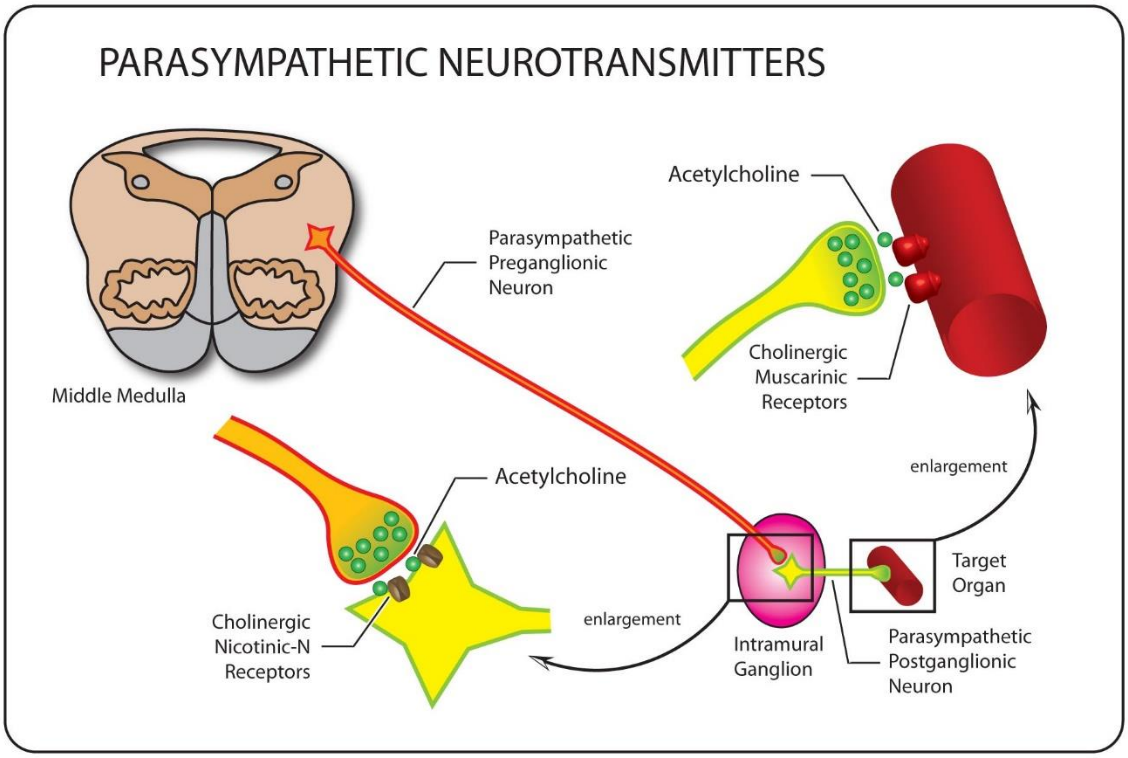

Figure 13.3 © 2014 David G. Ward, Ph.D.

- Parasympathetic preganglionic neurons release acetylcholine which acts on nicotinic-n (N-n) receptors on the ganglionic neurons
    - Binding of acetylcholine to N-n receptors usually cause sodium channels to open, leading to excitation.
- Most parasympathetic postganglionic fibers release acetylcholine which act on muscarinic cholinergic receptors on the target organs.
    - Cholinergic receptors are G-protein coupled and can cause either excitation or inhibition. Binding of acetylcholine to:
        - M_1/M_3 receptors causes calcium channels to open and potassium channels to close, leading to excitation and/or contraction.
        - M_2 receptors causes potassium channels to open leading to inhibition.

Table 13.1. Muscarinic and nicotinic cholinergic receptors

<table>
<tr><th>N-n receptors</th><th colspan="2">M-1/M-3 receptors</th><th>M-2 receptors</th></tr>
<tr><td>Acetylcholine binds to nicotinic-n receptors, opens sodium channels in dendrites, causing depolarization (stimulation)</td><td colspan="2">Acetylcholine binds to M-1 or M-3 receptors which are G-protein coupled receptors</td><td>Acetylcholine binds to M-2 receptors which are G-protein coupled receptor</td></tr>
<tr><td></td><td colspan="2">G-protein alpha is activated</td><td>G-protein alpha is activated</td></tr>
<tr><td></td><td colspan="2">Activated G-protein alpha activates phospholipase C</td><td>G-protein beta-gamma is released and binds to and opens potassium channels in the plasma membrane, causing hyperpolarization (inhibition)</td></tr>
<tr><td></td><td colspan="2">Phospholipase C catalyzes Phosphatidyl Inositol (PIP2) to Inositol Triphosphate (IP3) and to Diacylglycerol (DAG)</td><td></td></tr>
<tr><td></td><td>IP3 binds to and opens IP3 gated Ca^{++} channels in the endoplasmic reticulum, causing depolarization (stimulation) and/or contraction</td><td>DAG activates Protein Kinase C which phosphorylates and closes potassium channels in the plasma membrane, causing depolarization (stimulation)</td><td></td></tr>
</table>

Parasympathetic Actions on Organs of the Head:

The cranial ganglia of the head control organs of the head, as shown in Figure 13.4.

- Stimulation of the ciliary, sphenopalatine, submandibular, and otic ganglia, which connect to the eyes, nose, and salivary glands, causes
    - Constriction of the pupils by stimulating contraction of pupillary constrictor muscles (M-3)
    - Accommodation of the lens of the eye by stimulating contraction of ciliary muscles (M-3)
    - Secretion of tears by the lacrimal (tear) glands (M-3)
    - Secretion of mucus by the olfactory mucus glands (M-3)
    - Secretion of watery saliva by the submandibular and sublingual (salivary) glands (M-3)
    - Secretion of watery saliva by the parotid (salivary) gland (M-3)

Parasympathetic Actions on Thoracic / Abdominal Organs

The thoracic and abdominal intramural ganglia control organs of the thorax and abdomen, as shown in Figure 13.4.

- Stimulation of the thoracic intramural ganglia causes
  - Constriction of the respiratory airways by contraction of smooth muscle (M-3)
  - Decreases in heart rate by hyperpolarizing the SA node (M-2)
- Stimulation of the abdominal intramural ganglia causes
  - Increases in secretion of HCl and pepsinogen by gastric glands (M-1)
  - Increases in secretion of fluids by pancreatic exocrine glands (M-3)
  - Increases in secretion of fluids by intestinal glands (M-3)
  - Increases in contraction of the gallbladder by stimulating smooth muscle (M-3)
  - Increases in gastrointestinal motility by stimulating the smooth muscle of the digestive tract (M-3)

Parasympathetic Actions on Pelvic Organs

The pelvic intramural ganglia control organs of the pelvis as shown in Figure 13.4.

- Stimulation of the pelvic intramural ganglia causes
  - Contraction of the urinary bladder by stimulation of smooth muscle(M-3)
  - Defecation by stimulation of smooth muscle (M-3)
  - Erection by dilation of arterioles (M-3 receptors of endothelial cells: Nitric Oxide)

Summary of Parasympathetic Actions on Organs

The parasympathetic nervous system is most active when the body is at rest, involved in eating and digestion, or engaged in sexual activity.

Almost all actions involve stimulation of smooth muscle contraction or stimulation of glandular secretion. Most of these stimulatory actions, including constriction of bronchial tubes, salivation, and increased gastrointestinal motility, are mediated mainly by **M-3** receptors.

The remaining actions involve other mechanisms. Heart rate is decreased by hyperpolarizing the SA node, a process which is mediated by **M-2** receptors. Erection is caused by the inhibition of smooth muscle contraction in arterioles, which is caused by nitric oxide from the endothelium. The production of nitric oxide by endothelial cells is mediated by **M-3** receptors.

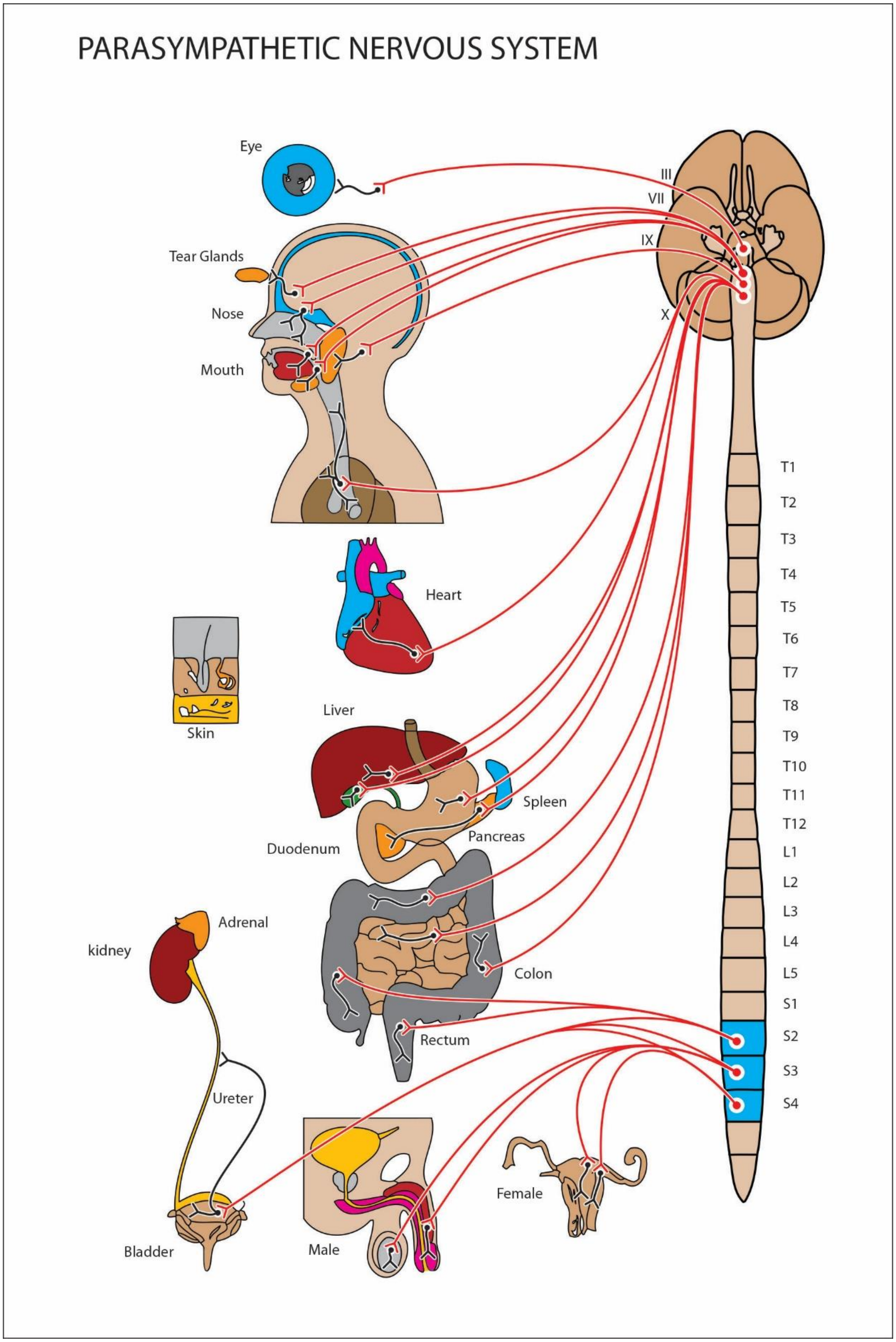

Figure 13.4 © 2014 David G. Ward, Ph.D.

Sympathetic Division

Spinal organization

The cell bodies of sympathetic preganglionic neurons (the first motor neurons in line) originate from the lateral horns of the thoracic spinal cord and from the first two segments of the lumbar spinal cord, as shown in Figures 13.5. The axons of the preganglionic neurons travel through spinal nerves.

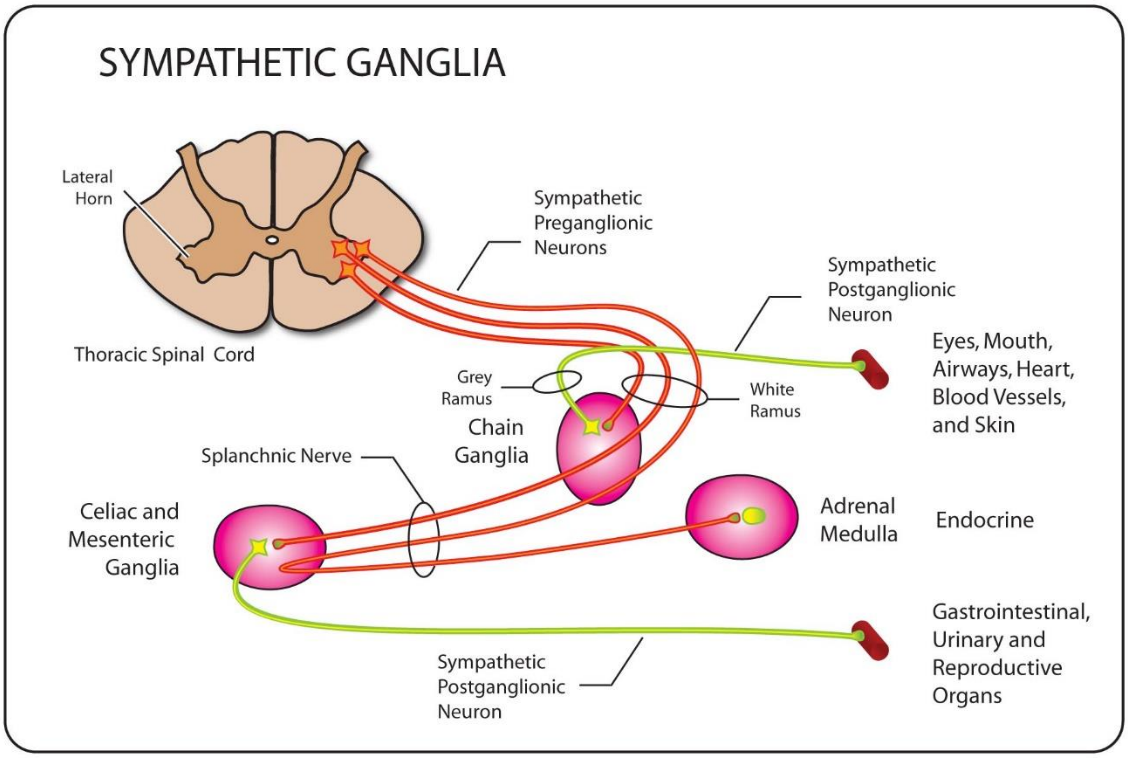

Figure 13.5 © 2014 David G. Ward, Ph.D.

- Preganglionic axons, controlling the head, thoracic organs, blood vessels of skeletal muscle, and accessory organs of skin, travel through spinal nerves and synapse on neurons in the chain ganglia.
- Preganglionic axons, controlling the abdominal and pelvic organs, travel through spinal nerves and synapse on ganglionic neurons in the celiac and mesenteric ganglia.
- Preganglionic neurons, controlling the adrenal gland, travel through spinal nerves and synapse on chromaffin cells and other ganglionic neurons of the adrenal medulla (“ganglion”).

Neurotransmitters

The actions of sympathetic preganglionic neurons and of the sympathetic postganglionic neurons depend on specific neurotransmitters and receptors. The organization of the sympathetic neurotransmitters is shown in Figure 13.6. The mechanisms of action of alpha and beta receptors are summarized in Tables 13.3 and 13.4.

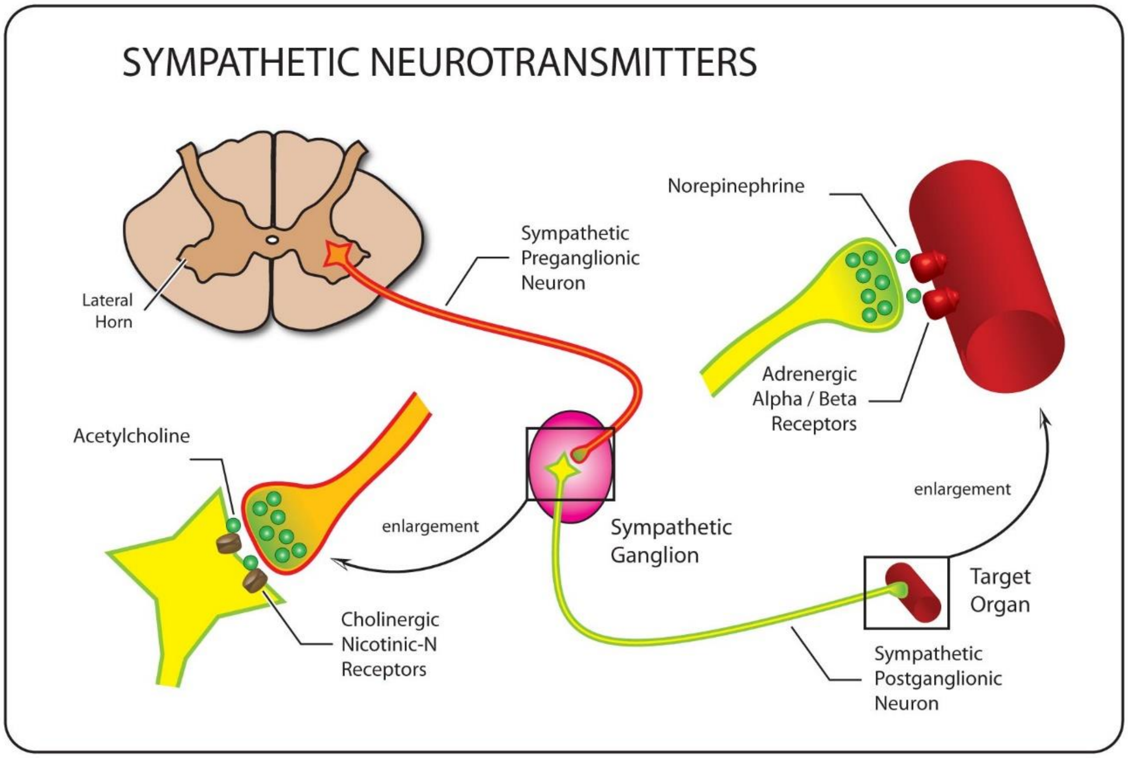

Figure 13.6 © 2014 David G. Ward, Ph.D.

- Sympathetic preganglionic neurons release acetylcholine, which in turn acts on nicotinic-n (N-n) receptors on the ganglionic neurons
  - Binding of acetylcholine to N-n receptors causes sodium channels to open, leading to excitation.
- Most Sympathetic postganglionic fibers release norepinephrine, which in turn acts on either alpha- or beta-adrenergic receptors on the target organs.
  - Adrenergic receptors are G-protein coupled and can cause either excitation or inhibition. Binding of norepinephrine to:
    - Alpha-1 receptors causes Ca^{2+} channels to open and K^+ channels to close, leading to excitation and/or contraction.
    - Beta-1 receptors causes Ca^{2+} and/or Na^+ channels to open, leading to excitation.
    - Beta-2 receptors causes Ca^{2+} to be removed from the cytosol, leading to inhibition and/or relaxation.
    - Beta-3 receptors causes the production of enzymes that break down fat.
- Some sympathetic postganglionic neurons secrete acetylcholine, which in turn acts on cholinergic muscarinic receptors.

Table 13.3. Alpha-1 and Alpha-2 adrenergic receptors.

<table>
<tr><th colspan="2">Alpha-1 and Alpha -2 postsynaptic receptors</th><th>Alpha-2 presynaptic and non-synaptic receptors</th></tr>
<tr><td colspan="2">Norepinephrine binds to alpha-1 receptors which are G-protein coupled receptors</td><td>Norepinephrine binds to alpha-2 receptors which are G-protein coupled receptors</td></tr>
<tr><td colspan="2">G-protein alpha is activated</td><td>G-protein alpha is activated</td></tr>
<tr><td colspan="2">Activated G-protein alpha activates phospholipase C</td><td>Activated G-protein alpha inhibits Adenyl Cyclase</td></tr>
<tr><td colspan="2">IP3 binds to and opens IP3 gated Ca^{++} channels in the Endoplasmic Reticulum</td><td>Without active Adenyl Cyclase ATP is not catalyzed to cAMP</td></tr>
<tr><td>IP3 binds to and opens IP3 gated Ca^{++} channels in the Endoplasmic Reticulum, causing depolarization (stimulation) and/or contraction</td><td>DAG activates Protein Kinase C which phosphorylates and closes potassium channels in the plasma membrane, causing depolarization (stimulation)</td><td>cAMP gated sodium and calcium ion channels are not opened, preventing depolarization (inhibition)</td></tr>
</table>

Table 13.4. Beta-1, Beta-2, and Beta-3 adrenergic receptors.

<table>
<tr><th>Beta-1 receptors</th><th>Beta-2 receptors</th><th>Beta-3 receptors</th></tr>
<tr><td>Norepinephrine binds to beta-1 receptors which are G-protein coupled receptors</td><td>Norepinephrine binds to beta-2 receptors which are G-protein coupled receptors</td><td>Norepinephrine binds to beta-3 receptors which are G-protein coupled receptors</td></tr>
<tr><td>G-protein alpha is activated</td><td>G-protein alpha is activated</td><td>G-protein alpha is activated</td></tr>
<tr><td>G-protein alpha activates Adenyl Cyclase</td><td>G-protein alpha activates Adenyl Cyclase</td><td>G-protein alpha activates Adenyl Cyclase</td></tr>
<tr><td>Adenyl Cyclase catalyzes the conversion of ATP to cAMP</td><td>Adenyl Cyclase catalyzes the conversion of ATP to cAMP</td><td>Adenyl Cyclase catalyzes the conversion of ATP to cAMP</td></tr>
<tr><td>cAMP activates Protein Kinase A</td><td>cAMP activates Protein Kinase A</td><td>cAMP activates Protein Kinase A</td></tr>
<tr><td>Protein Kinase A phosphorylates and opens sodium and calcium ion channels, causing depolarization (stimulation)</td><td>Protein Kinase A
1) among many actions, phosphorylates transport pumps that move calcium ions into the sarcoplasmic reticulum, preventing depolarization (inhibition) and contraction
2) phosphorylates enzymes involved in glucose metabolism</td><td>Protein Kinase A phosphorylates enzymes that break down lipids (lipolysis)</td></tr>
<tr><td colspan="3">cAMP is degraded by cAMP phosphodiesterase (a process inhibited by caffeine)</td></tr>
</table>

Superior Cervical Sympathetic Ganglion:

The superior cervical ganglion controls organs of the head, as shown in Figure 13.7.

- Stimulation of the superior cervical sympathetic ganglion:
    - Dilates pupils by stimulating pupillary dilator muscles (Alpha-1)
    - Suppresses accommodation of the lens by relaxing ciliary muscles (Beta-2)
    - Increases secretion of viscous saliva by the salivary glands (Alpha-1)
    - Increases secretion of enzymes by the salivary glands (Beta-1)

Cervical Sympathetic Ganglia and Upper Thoracic Chain Ganglia:

The superior, middle and inferior cervical ganglia in conjunction with the upper thoracic (1-4) chain ganglia control organs of the thorax, as shown in Figure 13.7.

- Stimulation of the cervical sympathetic ganglia and the upper thoracic chain ganglia:
    - Increases in heart rate and force of contraction (Beta-1)
    - Dilates the respiratory passageways by relaxing smooth muscle (Beta-2)

Most Sympathetic Chain Ganglia:

Most of the chain ganglia control blood vessels in skeletal muscles and skin, and control accessory organs of skin.

- Stimulation of the chain ganglia:
    - Increases blood flow to active skeletal muscle, by relaxing vascular smooth muscle (Beta-2)
    - Increases blood flow to skin, by relaxing vascular smooth muscle (Beta-2 and possibly Muscarinic - M-3*)
    - Decreases blood flow to inactive skeletal muscle, by contracting vascular smooth muscle (Alpha-1)
    - Decreases blood flow to skin, by contracting vascular smooth muscle (Alpha-1)
    - Causes erection of hair, by stimulation of smooth muscle (arrector pili) of hair follicles (Alpha-1)
    - Increases secretion of sweat, by stimulating sweat glands (Muscarinic - M-3*)

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* Some Sympathetic Postganglionic neurons secrete Acetylcholine. These neurons are often referred to as cholinergic sympathetic postganglionic neurons. Their targets are mainly in the skin, which include merocrine sweat glands and possibly the endothelium of blood vessels.

Celiac and Superior Mesenteric Ganglia:

The celiac, renal, and superior mesenteric ganglia control the abdominal organs, including the kidney, as shown in Figure 13.7.

- Stimulation of the celiac and superior mesenteric ganglia:
  - Decreases blood flow to gastrointestinal organs by contracting vascular smooth muscle (Alpha-1)
  - Decreases blood flow to the kidneys by contracting smooth muscle (Alpha-1)
  - Decreases gastrointestinal motility by relaxing the smooth muscle of the digestive tract (Alpha-2, Beta-2)
  - Increases secretion of renin by juxtaglomerular cells of the kidney (Beta-1)

Inferior Mesenteric Ganglion:

The inferior mesenteric ganglion controls the pelvic organs, as shown in Figure 13.7.

- Stimulation of the inferior mesenteric ganglion:
  - Relaxes the bladder by relaxing smooth muscle (Beta-2)
  - Relaxes the uterus by relaxing smooth muscle (Beta-2)
  - Contracts the uterus in pregnancy by contracting smooth muscle (Alpha-1)
  - Causes ejaculation by stimulating smooth muscle (Alpha-1)

Adrenal Medulla:

The adrenal medulla is a sympathetic ganglion organized such that the ganglionic neurons secrete their neurotransmitters directly into the blood. A chemical messenger traveling in the blood is called a hormone. As a result the adrenal medulla functions as an endocrine gland.

- Stimulation of the adrenal medulla causes a large secretion of epinephrine and a smaller secretion of norepinephrine.

Summary of Sympathetic Actions on Organs

The sympathetic nervous system is most active when the body is physically active.

Many actions involve stimulation of smooth muscle contraction. Most of these stimulatory actions, including constriction of blood vessels, are mediated mainly by **Alpha-1** receptors. However, some stimulatory actions, especially sweating, are mediated by **M-3** receptors.

Other actions involve inhibition of smooth muscle contraction. These inhibitory actions, including relaxation of blood vessels and bronchial tubes, are mediated mainly by **Beta-2** receptors.

A small number of remaining actions involve stimulation of cardiac muscle contraction, or stimulation of glandular secretions. These stimulatory actions, including increased heart rate and force of contraction, are mediated by **Beta-1** receptors.

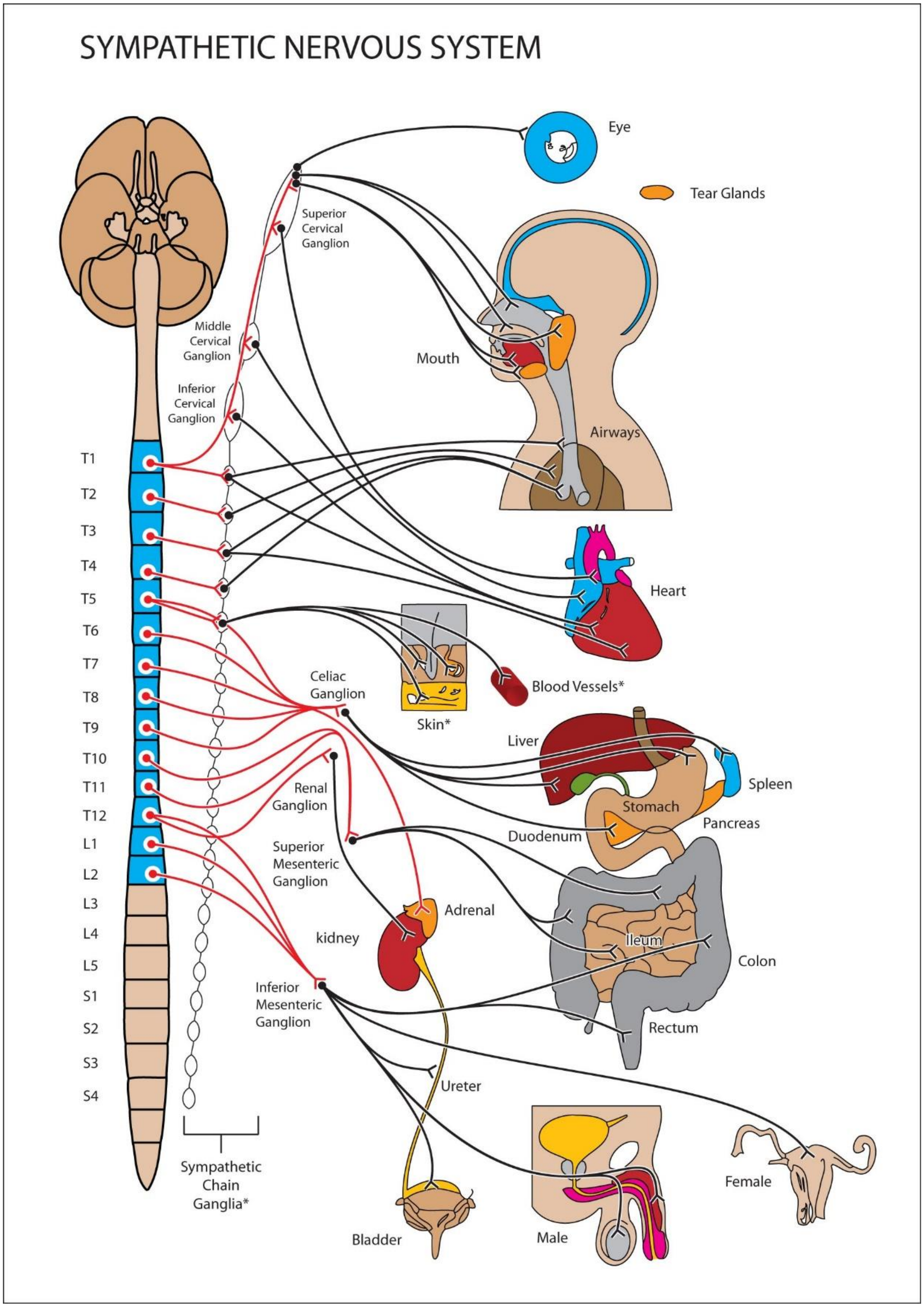

Figure 13.7 © 2014 David G. Ward, Ph.D.

Quiz Yourself

1-5. Matching

A) secrete mainly epinephrine
B) secrete norepinephrine
C) secrete acetylcholine

adrenal medullary cells 1) _____
sympathetic preganglionic neurons 2) _____
sympathetic postganglionic neurons 3) _____
parasympathetic preganglionic neurons 4) _____
parasympathetic postganglionic neurons 5) _____

6-10. Matching

A) parasympathetic division
B) sympathetic division

dilates pupils 6) _____
constricts pupils 7) _____
accommodates lens of eye 8) _____
increases gastrointestinal motility 9) _____
constricts gastrointestinal blood vessels 10) _____

11-15. Matching (cholinergic)

A) Nicotinic-m receptors
B) Nicotinic-n receptors
C) Muscarinic-1 receptors
D) Muscarinic-2 receptors
E) Muscarinic-3 receptors

GPCRs, ↑ PLC, ↑ IP3, ↑ Ca^{2+} in smooth muscle 11) _____
ligand gated Na+ channels in skeletal muscle 12) _____
GPCRs, ↑ PLC, ↑ IP3, ↑ Ca^{2+} in neurons 13) _____
ligand gated Na+ channels in neurons 14) _____
GPCRs, $G\beta\delta$ gated K^+ channels 15) _____

16-20. Matching (adrenergic)

A) beta-1 receptors
B) beta-2 receptors
C) beta-3 receptors
D) alpha-1 receptors
E) alpha-2 presynaptic receptors

GPCRs, ↑ adenyl cyclase, ↑ cAMP, ↑ PKA, ↑ Ca^{2+} pumps 16) _____
GPCRs, ↑ adenyl cyclase, ↑ cAMP, ↑ PKA, ↑ Ca^{2+}, Na^+ 17) _____
GPCRs, ↑ adenyl cyclase, ↑ cAMP, ↑ PKA, ↑ lipolysis 18) _____
GPCRs, ↓ adenyl cyclase, ↓ cAMP, ↓ Na^+, Ca^{2+} 19) _____
GPCRs, ↑ PLC, ↑ IP3, ↑ Ca^{2+} 20) _____

Fill in

21. _________________ preganglionic neurons originate mainly in spinal cord.

22. The ganglia of the ___________________ nervous system are typically in the target organs.

23. The sympathetic and parasympathetic postganglionic neurons contain _______________ receptors.

24. Sympathetic postganglionic neurons typically release _______________.

25. Parasympathetic postganglionic neurons typically release _______________.

Study Questions

1. Compare and contrast the organization, of the parasympathetic and sympathetic divisions of the autonomic nervous system.
2. Compare and contrast the neurotransmitters, and receptors of the parasympathetic and sympathetic divisions of the autonomic nervous system.
3. Compare and contrast some of the major organ responses to parasympathetic and sympathetic stimulation