General Physiology
Second semester 2023 2024
Lectures24
Functions of Adrenal Medulla and its relation to Sympathetic Nervosa system
Autonomic Reflexes
Central Regulation of Autonomic Reflexes

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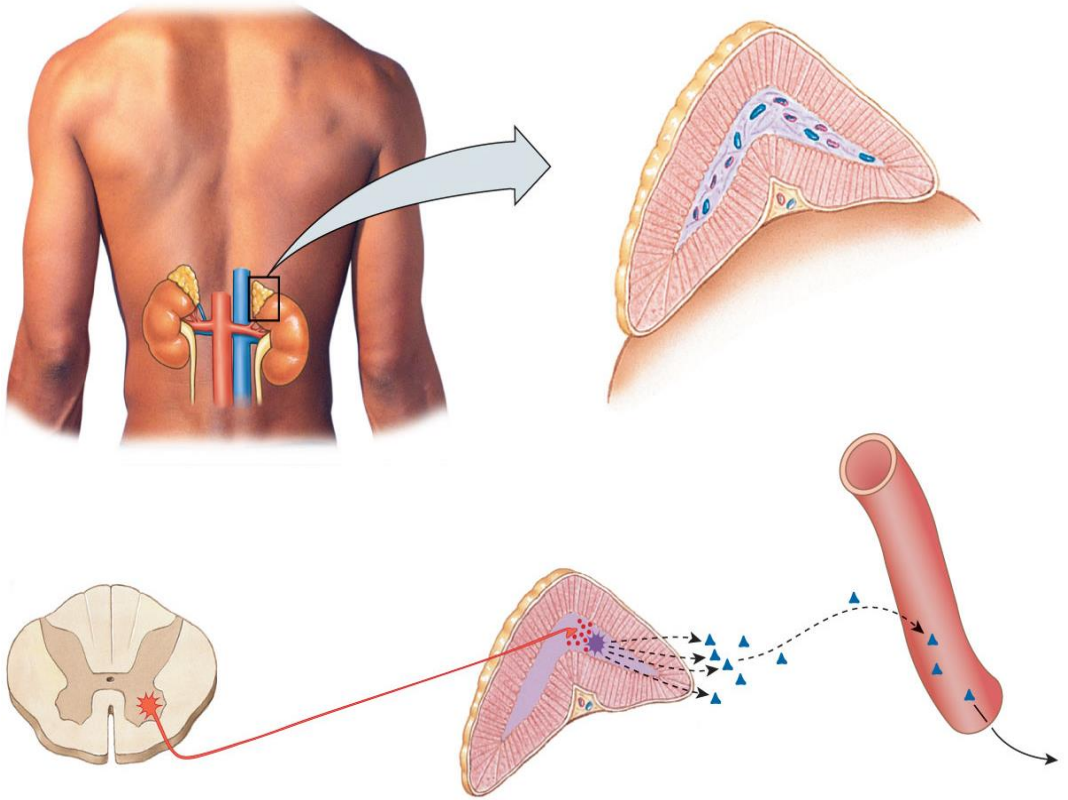
Lecture Objectives

- Describe the sympathetic innervation to adrenal medulla
- Identify the hormones released by adrenal medulla and their functions.
- Understand the sympathetic and parasympathetic tone.
- Identify central nervous system areas which influence the activity of autonomic nervous
- Briefly Identify the autonomic reflexes and list examples of theses reflexes
- Describe the stress and alarm response of the sympathetic nervous system.

Functional anatomy of adrenal medulla (Suprarenal gland)

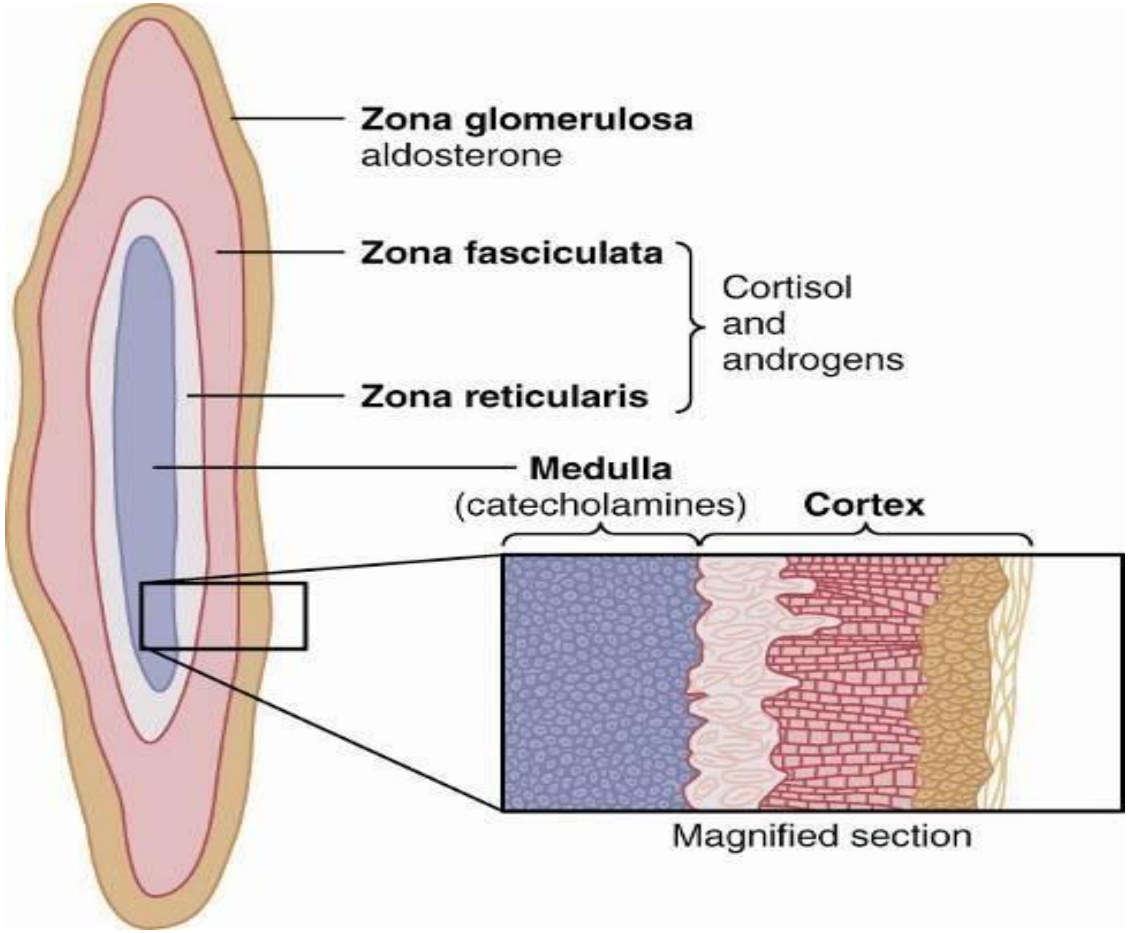
Two adrenal glands in the body and each gland is in close association with a kidney.
The adrenal glands are:

- Composed of
  - Adrenal medulla (the central 20%)
  - Adrenal cortex (80% of the gland).



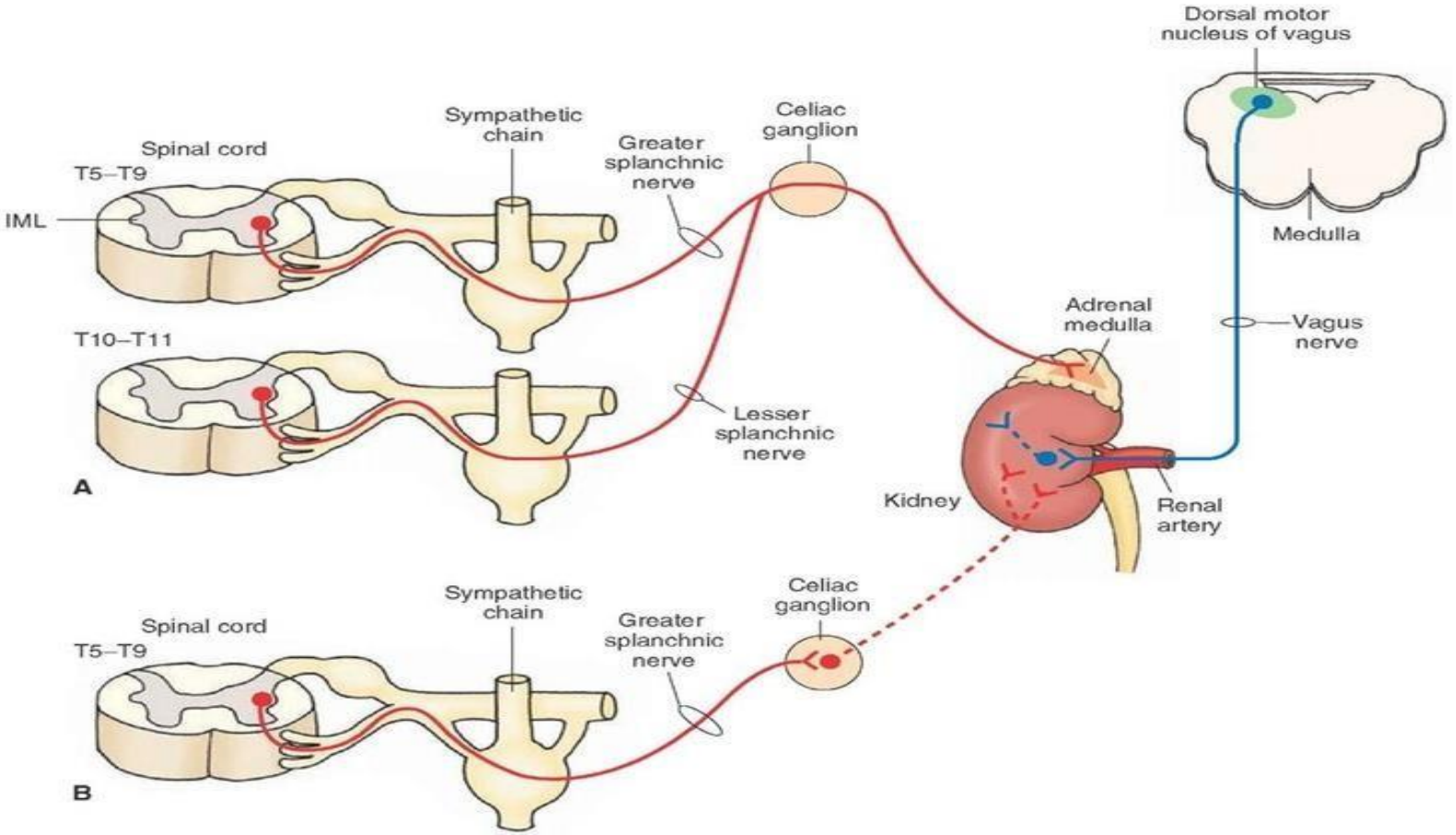
Functional anatomy of adrenal medulla

The medulla is functionally related to the sympathetic nervous system. It is derived from a subpopulation of neural crest cells.
It synthesizes and secretes **epinephrine**, **norepinephrine**, and **dopamine**(function?) in response to direct sympathetic stimulation. These hormones cause almost the same effects as direct stimulation of the sympathetic nerves.
The adrenal cortex is derived from mesodermal tissue and secretes **corticosteroids** . These hormones are synthesized from the cholesterol



Adrenal medulla and its Innervation by sympathetic nervous system

It receives preganglionic fibers mainly greater splanchnic nerve which terminates in the celiac ganglia



Release of adrenal medulla hormones and their time course of action

- The adrenal medulla release Catecholamines
- Catecholamines (NE, Epi and Dopamine) are amino acid-derived hormones, synthesized from the amino acid tyrosine by the medullary pheochromocyte (Chromaffin cells) in response to nicotinic cholinergic receptors stimulation. The type of cell that secretes dopamine is unknown
- Stimulation of the sympathetic nerves to the adrenal medullae causes release of large quantities of the hormones epinephrine (E) and norepinephrine (NE) into the circulating blood.
- 80% of the secretion is epinephrine and 20% is norepinephrine, although the relative proportions **can change** considerably under different physiological conditions
- Catecholamines do not cross the blood-brain barrier easily, therefore they exert their effects almost exclusively in peripheral tissues and not in the brain

Adrenal Catecholamines Continue

- 80% of the secretion is epinephrine and 20% is norepinephrine, although the relative proportions **can change** considerably under different physiological conditions.
- The circulating E and NE have almost the same effects on the different organs as the effects caused by direct sympathetic stimulation , except that the effects last 5 to 10 times as long because both hormones are removed from the blood slowly over a period of 2 to 4 minutes. (they have short half life)
- Most (>50%) of the catecholamines released circulate bound to albumin with low affinity

Major effects of Norepinephrine and Epinephrine

- **Increase alertness:** E and NE are equally potent in this regard, although in humans epinephrine usually evokes more anxiety and fear.
- **Increased rate and force of contraction of the heart muscle: this** is predominantly an effect of epinephrine acting through beta receptors.
- **Constriction of blood vessels:** norepinephrine, in particular, causes widespread vasoconstriction, through alpha adrenergic, resulting in increased resistance and hence arterial blood pressure.
- **Dilation of bronchioles: assists** in pulmonary ventilation.(B2 receptor effect)
- **Stimulation of lipolysis in fat cells:** this provides fatty acids for energy production in many tissues and aids in conservation of blood glucose. Reserve.
- **Increased metabolic rate:** oxygen consumption and heat production increase throughout the body in response to epinephrine. Medullary hormones also promote breakdown of glycogen in skeletal muscle to provide glucose for energy y production.
- **Dilation of the pupils:** particularly important in situations where human or animal are surrounded by conditions of low ambient light.
- **Inhibition of certain "non-essential" processes: an** example is inhibition of gastrointestinal secretion and motility .

Major effects of Norepinephrine and Epinephrine

- Epinephrine is a universal adrenergic receptor stimulator; and since it stimulates β receptors it causes powerful cardiac stimulation, mild rise in blood pressure, and grater metabolic effect (5-10 times) compared to that of norepinephrine
- The metabolic effects include an increase in BMR, ↑ glycogenolysisand gluconeogenesis (β2) in the liver and muscles, ↑ lipolysis (β1), and ↑ glucose and lactate release into the blood (hyperglycemia and hyperlactatemia). The metabolic effect of humoral catecholamine cannot be substituted by direct sympathetic stimulation as small proportion of all the cells in the body are innervated directly by sympathetic fibers.
- Chronic exposure to adrenergic receptor agonists can reduce the number of receptors in the plasma membrane because of decreased synthesis of the receptor (downregulation). Examples include β-agonist-promoted desensitization in asthma

Major effects of Norepinephrine and Epinephrine

- Most of the increase in fat utilization occurs during heavy exercise. This results almost entirely from release of E and NE by the adrenal medulla. Both hormones activate triglyceride lipase in fat cells → liberation of free fatty acids.
- There is basal secretion of E and NE by the adrenal medulla This basal rate of secretion maintains the blood pressure. The gland increases its secretion rate in **alarm** or **stress response**(= mass discharge of sympathetic system) such as during physical exercise, mental stress (anger, anxiety, pain), cold, hypoglycemia, hypoxia, bleeding, injury, etc.
- The overall reaction to the sudden release of catecholamines is known as the "**fight-or-flight**" response
- The regulatory sympathetic centers are mainly present in the brain stem reticular substance. However, signals from the hypothalamus and even from the cerebrum can modulate activities of all autonomic control centers.
- Pheochromocytomas are adrenal medullary tumors that mostly secrete NE. They cause episodic or sustained hypertension.
- Dopamine has positive inotropic effect (↑ systolic blood pressure but has no effect on diastolic blood pressure). Therefore, moderate doses are useful in treatment of traumatic and cardiogenic shock

Comparison Between Epinephrine and Norepinephrine responses

- Epinephrine causes almost the same effects as those caused by norepinephrine.

1. NE has greater affinity for alpha adrenergic receptors and Epinephrine has a higher affinity for beat adrenergic receptors

- Epinephrine Has a greater effect on cardiac stimulation than does norepinephrine.
- Epinephrine causes only weak constriction of the blood vessels in the muscles, in comparison with much stronger constriction caused by norepinephrine.
- The effects of Epinephrine on metabolism is 5 to 10 times as great as norepinephrine.
- Example of metabolic effects

  glycogenolysis in the liver and muscle and glucose release into the blood.

Advantage of Adrenal Medullary Secretion

- The simultaneous organ stimulation directly by sympathetic nerves and indirect by the adrenal medullary hormones support each other (synergistic effect)
- Adrenal medullary epinephrine and norepinephrine stimulates structures of the body that are not innervated by direct sympathetic fibers

Sympathetic and Parasympathetic Tone

- Normally, the sympathetic and parasympathetic systems are **continually active**, and the basal rates of activity are known, respectively, as **sympathetic tone and parasympathetic tone**.
- The increase or decrease in the tone can increase or decrease in the activity of the stimulated organ.
- Examples
- Increase sympathetic tone can cause vasoconstriction and decrease of sympathetic tone vasodilation of arterioles
- Gastric motility is affected by change in parasympathetic tone
- Heart rate is increased or decrease by changing parasympathetic and sympathetic tone .

Sympathetic and Parasympathetic Tone

- Under different physiological conditions , the activity of one autonomic nervous system subdivision can dominate the other.
- For example : the sympathetic system dominates during stress response, while parasympathetic system dominates in quiet and restful circumstances (Rest and digest).
- Sympathetic tone Caused by Basal Secretion of Epinephrine : much of the overall tone of the sympathetic nervous system results from basal secretion of epinephrine and norepinephrine in addition to the tone resulting from direct sympathetic stimulation
- Removal of the sympathetic or parasympathetic tone by denervation results in **denervation supersensitivity**. This mechanism is believed to be due to up-regulation of the adrenergic or cholinergic receptors

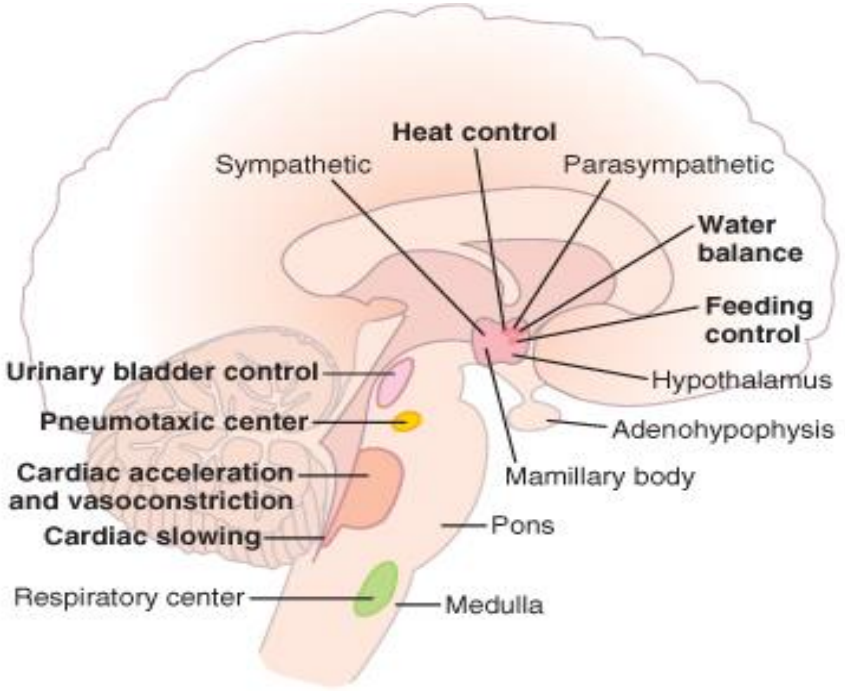
Local Vs. Mass Stimulation of the Sympathetic and Parasympathetic Systems

- **Mass discharge of sympathetic nervous system wide spread activity in all parts of the SNS**
- The result is a widespread reaction throughout the body called the **alarm** or **stress response**
  - Localized activation occurs in isolated portions of the sympathetic nervous system. For example , thermoregulation : control of sweating and vascular blood flow in the skin.
- The parasympathetic system usually causes specific localized responses. Example is the salivation in the mouth upon stimulation of touch receptors on the mouth by food .
- However, there is often **association** between closely allied parasympathetic functions. Example; urinary bladder and rectal emptying reflexes

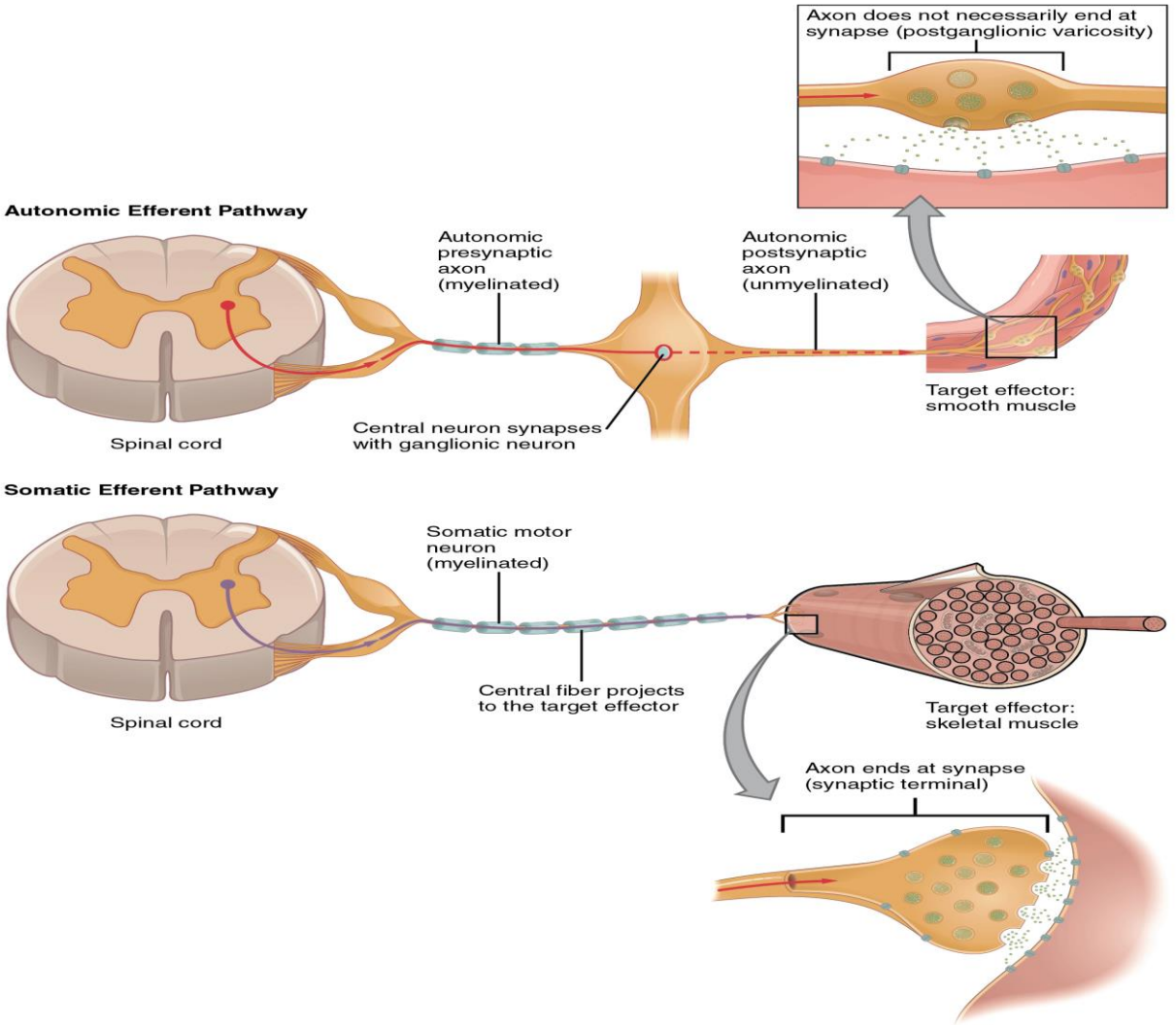
The Alarm or Stress Response of the Sympathetic Nervous System

- **The stress response increases the ability of the body to perform vigorous muscle activity in many ways, including:**
  1. **Increased arterial pressure.**
  2. **Increased blood flow to active muscles concurrent with decreased blood flow to organs such as the gastrointestinal tract and the kidneys that are not needed for rapid motor activity.**
  3. **Increased rates of cellular metabolism throughout the body.**
  4. **Increased blood glucose concentration.**
  5. **Increased glycolysis in the liver and in muscle.**
  6. **Increased muscle strength.**
  7. **Increased mental activity.**
  8. **Increased rate of blood coagulation.**
- **The sympathetic system is especially strongly activated in many emotional states. For instance, in the state of rage.**
- **The sympathetic alarm reaction is also called the fight-or-flight reaction.**

Higher central nervous system Pathwaysthat control autonomic responses



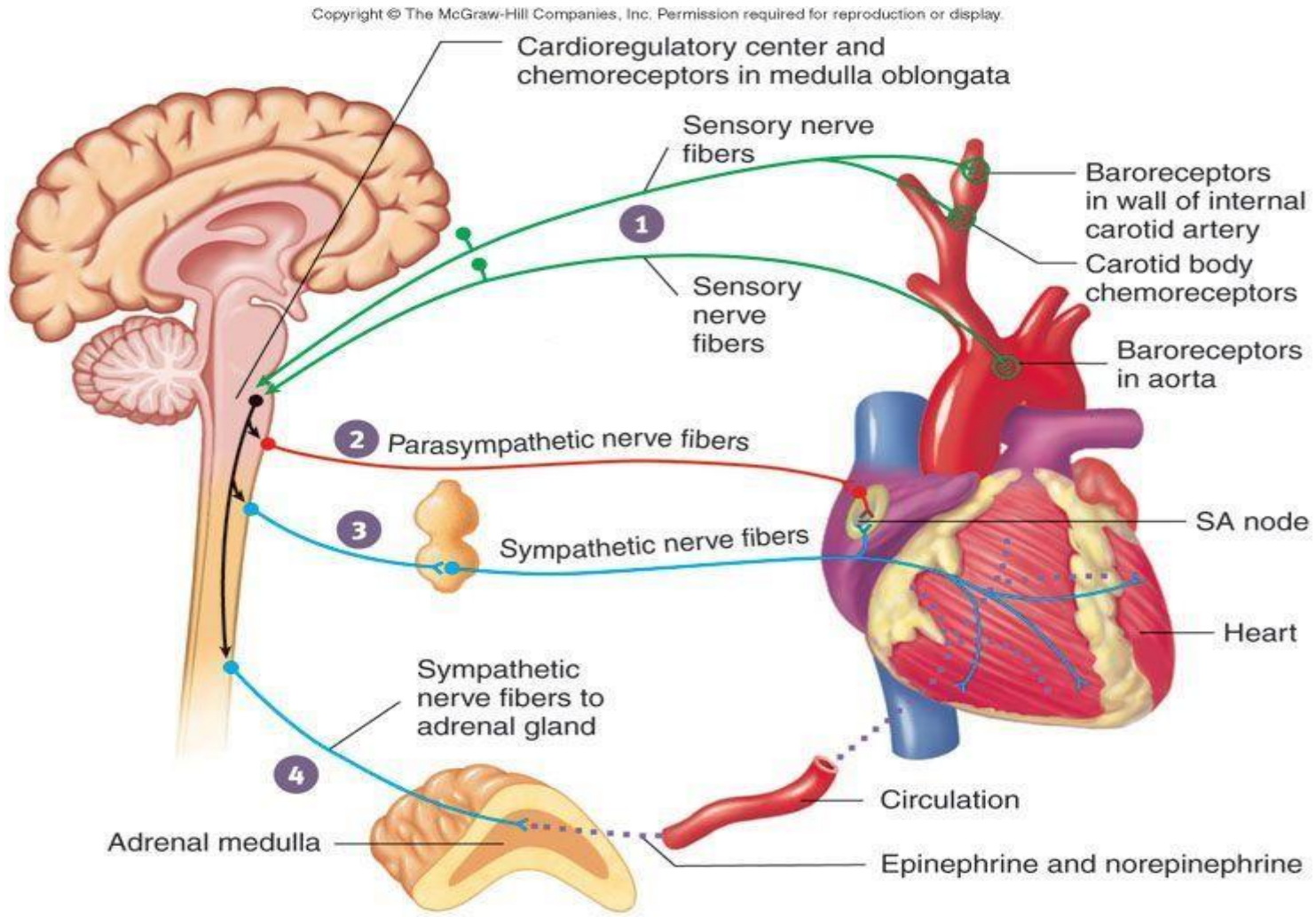
Autonomic vs Somatic Reflexes



Autonomic reflexes

- Cardiovascular Autonomic Reflexes For example Barorecptor reflex .
- Gastrointestinal Autonomic Reflexes Defecation reflex
- Pupil reflex
- Micturition reflex : Emptying of the urinary bladder
- Sexual reflexes Erection and ejaculation

Baroreceptor autonomic reflex



Disturbances Related to Autonomic Involvement

- 1- Horner's syndrome:
    - Is a unilateral enophthalmos, ptosis, miosis, and flushing of the face often caused by an ipsilateral involvement of the sympathetic fibers in the cervical sympathetic chain or upper thoracic cord.
- 2- Hirschsprung's disease (megacolon):
    - Consists of a tremendous dilatation of the colon, with chronic constipation. It is associated with congenital lack of parasympathetic ganglia and the existence of abnormal fibrils in the apparently normal segment of large bowel wall
- 3. Dysautonomia
    - Autonomic failure
    - Autonomic neuropathy