Autonomic nervous system

Sompol Tapechum, M.D., Ph.D.
Department of Physiology
Faculty of Medicine Siriraj Hospital

Objectives

เมื่อจบบทเรียน นักศึกษาสามารถ

1. บอกความแตกต่างระหว่าง Autonomic และ Somatic nervous system ได้
2. บอกชนิดและองค์ประกอบของ Autonomic nervous system แต่ละชนิดได้
3. อธิบายกลไกการทำงานของ Autonomic nervous system ได้
4. บอกชนิดของสารสื่อประสาทและตัวรับที่ autonomic ganglion และ neuro-effector junction ของระบบประสาท sympathetic และ parasympathetic ได้
5. บอกหน้าที่ของ Autonomic nervous system ต่ออวัยวะต่างๆ ได้ทั้งหมดได้
Nervous system

Central nervous system (CNS)
- cerebrum
- cerebellum
- spinal cord

Peripheral nervous system (PNS)
- brachial plexus
- intercostal nerve
- radial nerve
- median nerve
- ulnar nerve
- lumbar plexus
- sciatic nerve
- common peroneal nerve
- superficial peroneal nerve
- sacral plexus
- digital nerve

Peripheral nervous system (PNS)

Peripheral nervous system
- Sensory nerves
- Motor nerves

Somatic nervous system

Autonomic nervous system (ANS)

Voluntary organs:
- Skeletal muscle

Involuntary organs:
- Smooth muscle
- Cardiac muscle
- Glands: exocrine, endocrine
Somatic nervous system

- Motor nerve to skeletal muscles
- "Motor neurons"
  - Anterior horn of spinal cord
  - Brainstem motor nuclei
- Efferent pathways
  - Single neuron (fiber)
  - Type A, long

Somatic nervous system: Neurotransmitter and receptor

- Neuromuscular junction or motor end-plate
- Neurotransmitter: Acetylcholine (Ach)
- Postsynaptic receptor: Nicotinic ACh receptors (ionotropic receptor, ligand-gated channel)

- Effects:
  - Opening of receptor channels
  - Na⁺ influx
  - Membrane depolarization (fast EPSP)
Somatic nervous system:

Functions

- Stimulation of somatic nervous system always causes muscle contraction.
- Voluntary movements
- Reflexive movements

Somatic Reflex Arc

1. Sensory Receptor
2. Afferent (sensory) neuron
3. Interneuron
4. Efferent (motor) neurons
5. Effector Organ

- In the peripheral reflex, a sensory neuron is excited by a receptor that detects stimuli in the quadriceps muscle and sends a signal to the spinal cord. The action of the sensory neuron is split: one branch fibers stimulate motor neurons in the quadriceps, causing the muscles to contract and extend the leg. The other branches fiber stimulates an interneuron which excites motor neurons in the hamstrings.
Autonomic nervous system (ANS)

- Motor nerves to
  - Cardiac muscle
  - Smooth muscle
  - Glands
- Divisions of Autonomic nervous system
  - Sympathetic nervous system
  - Parasympathetic nervous system
  - Enteric nervous system

Autonomic nervous system: Structure

- Ganglion = collection of neurons outside CNS
Autonomic ganglion: Ganglionic transmission

- Both sympathetic and parasympathetic use the same ganglionic transmission
  - Preganglionic fibers release Acetylcholine (ACh)
  - Postsynaptic receptor: Nicotinic ACh receptor
  - Postsynaptic response: Fast EPSP

- Actually, there are other neurotransmitters released at ganglia
  - Involve both fast and slow synaptic transmission
Nicotinic ACh receptors

- Permeable to Na\(^+\) and K\(^+\)
- Response with fast EPSP

**Note**

- Neuronal (N\(_N\)) and muscular (N\(_M\)) type nicotinic receptors are distinct pharmacologically
- Antagonist for N\(_N\) are trimethophan and hexamethonium

Neuro-effector junction

- No specialized presynaptic sites. no active zones
- No specialized postsynaptic sites
- Postsynaptic nerve endings have several swellings (Varicosities)
- Postsynaptic nerve endings are several hundred nanometers from the effectors
  - more diffuse control over target tissue

**En passant**

- **Neurotransmitters**
  - Sym: Norepinephrine (NE)
  - Parasymp: Acetylcholine
End organ responses

- Most organs supplied by ANS have spontaneous activity
- Therefore, the role of autonomic nervous system is to modulation
- Responses can be either excitation or inhibition

![EKG](image)

Characters of ANS responses

- **Mass discharge**: preganglionic fiber synapses with more than one postganglionic neurons
- **Dual innervation**:
  - most organs receive both sympathetic and parasympathetic fibers
  - Sympathetic and parasympathetic responses are always opposite
ANS functions

- Contributes to **homeostasis** response to internal environmental changes or external demand
  - **Visceral functions** (smooth muscle, cardiac muscles, exocrine glands)
  - **Behavioral response**
    - Sympathetic: fight or flight
    - Parasympathetic: rest and digest
  - **Endocrine functions**: hormonal response

---

**Autonomic nervous system: Functions**

- Autonomic responses are involuntary (reflex responses)

---

**Baroreceptor Reflex**
(control of Cardiovascular system)
Autonomic reflex arc

Autonomic Reflex Arc

1. Visceral receptor
2. Afferent neurons
   (Interneuron)
3. Efferent neurons
   • Preganglionic
   • Postganglionic
4. Effector

Afferent

<table>
<thead>
<tr>
<th>Somatic</th>
<th>Autonomic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory receptors</td>
<td>Skin, muscle, bone, joint</td>
</tr>
<tr>
<td></td>
<td>Visceral organs, blood vessels</td>
</tr>
<tr>
<td>Sensory neurons</td>
<td>Dorsal root ganglia, cranial nuclei</td>
</tr>
<tr>
<td></td>
<td>Dorsal root ganglia, cranial nuclei</td>
</tr>
<tr>
<td>Receptors</td>
<td>Present</td>
</tr>
<tr>
<td>Pain</td>
<td>Present</td>
</tr>
<tr>
<td>Temperature</td>
<td>Present</td>
</tr>
<tr>
<td>Touch</td>
<td>Present</td>
</tr>
<tr>
<td>Proprioceptors</td>
<td>Sparsely distributed</td>
</tr>
<tr>
<td>Special receptors</td>
<td>Few</td>
</tr>
<tr>
<td></td>
<td>Few</td>
</tr>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Osmoreceptors, baroreceptors, chemoreceptors</td>
</tr>
</tbody>
</table>
### Efferent (Motor pathways)

<table>
<thead>
<tr>
<th>Motor neurons</th>
<th>Somatic</th>
<th>Autonomic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior horn cells of spinal cord</td>
<td>Lateral horn of spinal cord</td>
<td></td>
</tr>
<tr>
<td>Some cranial motor nuclei</td>
<td>Sym: Thoracolumbar</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Parasymp: Craniosaral</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Numbers of neurons in efferent pathway</th>
<th>One</th>
<th>Two</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preganglionic</td>
<td>Postganglionic</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effector organs</th>
<th>Skeletal muscle</th>
<th>Smooth muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiac muscle</td>
<td>Glands: exocrine, endocrine</td>
</tr>
</tbody>
</table>

### Sympathetic nervous system: Preganglionic fibers
- Thoracolumbar outflow (C₈ or T₁- L₃ or L₄)
- Cells are in intermediolateral column of spinal cord
- Type B fiber. Short
- Along ventral root of spinal nerve
- Neurotransmitter release: Acetylcholine (ACh) = cholinergic fiber
- Divergence (1:10)
Sympathetic nervous system: Postganglionic fibers

- Sympathetic ganglia
  - paravertebral
  - prevertebral
- Type C fiber. Long
- Along spinal nerves or branches of vessels
- Neurotransmitter released: Norepinephrine (NE) = adrenergic fiber
- Exception
  - releases ACh at sweat glands and blood vessels in skeletal muscle

Parasympathetic nervous system: Preganglionic fibers

- Preganglionic neurons
  - Craniosacral outflow (brainstem and sacral spinal cord S2-S4)
  - Type B fiber, Long
- Neurotransmitter release: ACh (cholinergic fiber)
Parasympathetic nervous system: Postganglionic fibers

- Postganglionic neurons
  - Parasympathetic ganglia are near or within visceral organ
  - Type C fiber, Short
  - Neurotransmitter release: ACh (cholinergic fiber)
  - Pre:Post = 1:3
Autonomic nervous system: Synaptic transmission
Autonomic transmission

Sympathetic nervous system:
Presynaptic terminal

Postganglionic neurons
Norepinephrine (NE)
- Synthesized in nerve terminal (varicosities)
- Precursor: Tyrosine
- Termination: Reuptake
Sympathetic nervous system:
End organ receptors

- Receptors for norepinephrine and epinephrine - adrenergic receptors or adrenoceptor
- Metabotropic receptors: G-protein couple receptors ➔ Slow postsynaptic potential
- There are at least 4 types: \( \alpha_1, \alpha_2, \beta_1 \) and \( \beta_2 \)

<table>
<thead>
<tr>
<th>Second messenger</th>
<th>( \alpha_1 )</th>
<th>( \alpha_2 )</th>
<th>( \beta_1 )</th>
<th>( \beta_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood vessels</td>
<td>IP3</td>
<td>↓cAMP</td>
<td>↑cAMP</td>
<td>↑cAMP</td>
</tr>
<tr>
<td>GI Sphincter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presynaptic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>terminal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
<td></td>
<td>Airway, GI</td>
</tr>
<tr>
<td>Urogenital</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agonist</td>
<td>Clonidine</td>
<td>Isoproterenol</td>
<td>Isoproterenol</td>
<td>Isoproterenol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dobutamine</td>
<td>Terbutaline</td>
<td>Terbutaline</td>
</tr>
<tr>
<td>Antagonist</td>
<td>Prazosin</td>
<td>Propanolol</td>
<td>Propanolol</td>
<td>Propanolol</td>
</tr>
</tbody>
</table>

Adrenergic receptor: \( \alpha_1 \)
Adrenergic receptor: α2 and β

Cardiac muscle contraction:
Role of cAMP (β adrenergic receptor)
Smooth muscle contraction:
Role of cAMP (\(\beta\) adrenergic receptor)

Parasympathetic nervous system:
Presynaptic terminal

Postganglionic neurons
Acetylcholine (ACh)
- Synthesized in nerve terminal
- Precursor: acetyl CoA + Choline
- Termination: acetylcholine esterase
Parasympathetic nervous system: End organ receptors

- **Muscarinic receptors**: G protein couple
- **Slow postsynaptic potential**

<table>
<thead>
<tr>
<th></th>
<th>M1</th>
<th>M2</th>
<th>M3</th>
<th>M4</th>
<th>M5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second messenger</strong></td>
<td>IP3</td>
<td>DAG</td>
<td>IP3</td>
<td>DAG</td>
<td>IP3</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td>CNS, Ganglia</td>
<td>Heart</td>
<td>Glands, Smooth muscle</td>
<td>CNS</td>
<td>CNS</td>
</tr>
<tr>
<td><strong>Agonist</strong></td>
<td>Muscarine, Pilocarpine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antagonist</strong></td>
<td>Atropine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Muscarinic receptors: M2 (Heart)

- Decrease cAMP
Muscarinic receptors: M2 (Heart)
- Opening of K⁺ channels ==> membrane hyperpolarization

Muscarinic receptors: M3
- Second messengers: IP3 and DAG
- Increase intracellular Ca²⁺
Enteric nervous system (ENS)

- Neural network in GI tract
  - **Myenteric** (Auerbach’s) plexus: between muscular layers
  - **Submucosal** (Meissner's) plexus: in submucosa
- Consist of 80-100 million neurons, both sensory and motor neurons arrange as network of ganglia
- Can function independent of CNS control
  - GI movement
  - Secretory function
Enteric nervous system: Structure

Enteric nervous system: Reflex Pathway

Serotonin receptor antagonist: Ondansetron
Enteric nervous system:
Peristalsis

- Peristalsis - pattern of smooth muscle contraction that propels content distally in GI tract

Enteric nervous system:
Central control
Higher control of ANS: Hypothalamus

- Head of ANS
- Homeostasis: maintains body at precise value; “set-point”
- Input to hypothalamus
  - Visceral afferent
    - Vagus n. → nucleus solitary tract
    - Spinal cord → reticular formation
  - Limbic: regulation of behavior
- Output from hypothalamus
  - ANS: sympathetic and parasympathetic preganglionic neurons
  - Endocrine

Autonomic control: Heart

- Sympathetic
  - SA nodes: increase heart rate ($\beta_1$)
  - Cardiac muscle: increase contractility ($\beta_1$)
- Parasympathetic
  - SA nodes: decrease heart rate (M2)
  - Cardiac muscle: decrease contractility (M2)
Higher control of ANS: Brainstem centers

Autonomic control: Heart: Baroreceptor reflex

- Increase blood pressure $\Rightarrow$ increase carotid sinus activity to
- Activation of neurons in nucleus ambiguous (parasympathetic)
- Inhibition of neuron in ventrolateral medullar (sympathetic)
Micturition reflex: rest and filling

- Sympathetic
- Somatic

Micturition reflex: Bladder full

- Afferent
- Parasympathetic
Clinical correlation

- Signs of ANS dysfunction
  - Impairment of blood pressure control
    - Postural hypotension
    - Cold pressor test (normal if BP increase)
    - Norepinephrine infusion ➔ supersensitivity
  - Impairment of Heart rate control
    - Normally, carotid massage should increase HR
  - Defective sweating and skin temperature
  - GI dysfunction: gastroparesis, vomiting
  - Micturition problem
  - Sexual impotence

Autonomic failure

- Malfunction of the ANS resulted from an imbalance between the sympathetic and parasympathetic divisions.
- Aging, DM, stroke and Parkinson's disease
- Dizziness or lightheaded
- The most common signs of ANS impairment are
  - a drop in blood pressure when a person is standing or stands up suddenly (orthostatic hypotension); or
  - a drop in blood pressure within one hour of eating a meal (postprandial hypotension).
Horner’s syndrome

- Destruction of superior cervical ganglia
  - Ptosis
  - Miosis
  - Endophthalmos
  - Anhydrosis

- Cancer involving upper part of lung

Denervation supersensitivity

- Chronic lesion of sympathetic postganglionic neurons
- Up regulation of adrenergic receptors in end organs
- Increase response to circulating NE and E
Autonomic control: Eyes

**Sympathetic**
- Radial muscle of iris contraction ($\alpha_1$) Midriasis
- Circular muscle of iris contraction ($M_3$) Miosis
- Ciliary muscle contraction ($M_3$) near vision

**Parasympathetic**
- Ciliary epithelium Contraction ($\beta$)
- Ciliary muscle Contraction ($M_3$)

---

Autonomic control: Vascular and airway smooth muscle

- **Vascular smooth muscle**
  - Sympathetic
    - Skin, splanchnic vessels Contraction ($\alpha_1$)
    - Vessels in skeletal muscle Relaxation (Muscarinic)
  - Parasympathetic
    - Endothelial cells Release EDRF ($M_3$) (EDRF=endothelial derived relaxing factor vessel relax)
- **Airway smooth muscle**
  - Sympathetic Relaxation ($\beta_1$)
  - Parasympathetic Contraction ($M_3$)
Autonomic control: GI smooth muscle

- Sympathetic
  - GI smooth muscle: Relaxation (β2)
  - GI sphincter: Contraction (α1)
- Parasympathetic
  - GI smooth muscle: Contraction (M3)
  - GI sphincter: Relaxation

Autonomic control: Genitourinary

<table>
<thead>
<tr>
<th></th>
<th>Sympathetic</th>
<th>Parasympathetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder Wall</td>
<td>Relaxes</td>
<td>β2 Contracts</td>
</tr>
<tr>
<td>Sphincter</td>
<td>Contracts</td>
<td>α1 Relaxes</td>
</tr>
<tr>
<td>Uterus</td>
<td>Relaxes</td>
<td>β2 Contracts</td>
</tr>
<tr>
<td>Pennis, Seminal vesicles</td>
<td>Contracts</td>
<td>α Erection</td>
</tr>
<tr>
<td></td>
<td>Ejaculation</td>
<td>α Erection</td>
</tr>
</tbody>
</table>
Autonomic control:
Others

- Glands (salivary, GI, lacrimal)
  - Sympathetic: Decrease secretion
  - Parasympathetic: Increase secretion

- Endocrine
  - Sympathetic
    - Kidney: Increase renin release
    - Pancreatic β cell: Decrease insulin secretion

- Metabolic functions
  - Sympathetic
    - Liver: Increase gluconeogenesis/glycogenolysis
    - Fat: Increase lipolysis

Salivary glands

- Parasympathetic
  - Increase water content

- Sympathetic
  - Increase protein content