Organization of Nervous System:

**Nervous System**

- **Central nervous system** (CNS)
  - Brain
  - Spinal cord
- **Peripheral nervous system** (PNS)
  - Motor output
  - Sensory input

- Motor division (Efferent)
- Sensory division (Afferent)

"self governing"

**Autonomic Nervous System**
- (Involuntary; smooth & cardiac muscle)
- Stability of internal environment depends largely on this system

**Somatic Nervous System**
- (Voluntary; skeletal muscle)

Comparison of Somatic vs. Autonomic:

<table>
<thead>
<tr>
<th>Cell body location</th>
<th>NTs</th>
<th>Effector organs</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatic NS</td>
<td>ACh</td>
<td>Skeletal muscle</td>
<td>+ Stimulatory</td>
</tr>
<tr>
<td>Autonomic NS</td>
<td>ACh</td>
<td>Smooth muscle, glands, cardiac muscle</td>
<td>+ - Stimulatory or inhibitory (depends on NT and NT receptor Type)</td>
</tr>
</tbody>
</table>

Ganglion:
- A group of cell bodies located in the PNS

ACh = Acetylcholine

NE = Norepinephrine
Organization of Nervous System:

Nervous system

Integration

Central nervous system (CNS) → Peripheral nervous system (PNS)

Brain → Spinal cord

Motor output → Sensory input

Motor division (Efferent) → Sensory division (Afferent)

Autonomic Nervous System (Involuntary; smooth & cardiac muscle) → Somatic Nervous System (Voluntary; skeletal muscle)

Sympathetic division → Parasympathetic division

Divisions of Autonomic Nervous System (ANS):

1) **Sympathetic Division:** ("fight or flight")
   - Readies body for stressful situations
     - Heightens mental alertness
     - ↑ metabolic rate
     - Activates energy reserves
     - Dampens non-essentials (e.g., digestion)
     - ↑ heart rate / blood pressure
     - ↑ respiratory rate / bronchiole dilation
     - Activates sweat glands

2) **Parasympathetic Division:** ("rest and digest")
   - Conserves energy at rest
     - ↓ metabolic rate
     - ↓ heart rate / blood pressure
     - ↑ digestive gland secretions
     - ↑ digestive motility / blood flow
     - Stimulates defecation / urination
Sympathetic Division Anatomy:

- Sympathetic pathways have short preganglionic fibers and long postganglionic fibers
  - Preganglionic fibers originate in spinal cord between cord segments T1 – L2
  - Autonomic ganglia located close to spinal cord (arranged as sympathetic chain)
    - 23 ganglia / chain (3 cervical, 11 thoracic, 4 lumbar, 4 sacral, 1 coccygeal)

Pathways in sympathetic chain:

1) Terminate directly in sympathetic chain
   - Postganglionic axons exit out gray ramus communicans
2) Ascend / descend several segments before terminating
   - May ascend / descend to ganglia located outside T1 – L2

Cervical ganglia: (fed via T1 – T4)
   - Serve head / thorax

Sacral ganglia: (fed via T12 – L3)
   - Serve genitalia / urinary bladder
Sympathetic Division Anatomy:

Pathways in sympathetic chain:
3) Exit sympathetic chain before terminating in collateral (prevertebral) ganglia

• Form splanchnic nerves (fed via T5 – L2)

Celiac ganglion:
Serves upper abdominal cavity
  • Pass-through point for splanchnic nerve feeding adrenal medulla

Mesenteric ganglia:
Serve lower abdominal cavity

Parasympathetic Division Anatomy:

• Sympathetic pathways have long preganglionic fibers and short postganglionic fibers
  • Terminal ganglia located near effector tissue
  • Preganglionic fibers originate in brain stem and S2 – S4:
    • Oculomotor Nerve (III)
      • Ciliary ganglia: Pupillary sphincters / ciliary muscles
    • Facial Nerve (IV)
      • Pterygopatine ganglia: Nasal / lacrimal glands
      • Submandibular ganglia: Salivary glands
    • Glossopharyngeal Nerve (IX)
      • Otic ganglia: Salivary gland
    • Vagus Nerve (X)
      • Intramural ganglia: Visceral organs
    • Sacral Segments (S2 – S4):
      • Intramural ganglia: Large intestine / bladder / genitalia

90% of PNS fibers
ANS Physiology:
Fiber Types:

- **Cholinergic Fibers**: Synthesize / secrete acetylcholine (NT)
  - All preganglionic fibers (sympathetic and parasympathetic divisions)
  - Postganglionic fibers of **parasympathetic division**

- **Adrenergic Fibers**: Synthesize / secrete norepinephrine (NT)
  - Postganglionic fibers of **sympathetic division** (sans sweat glands / piloerector muscles)

Synthesis of Neurotransmitters:

- NTs synthesized / stored in varicosities of nerve fibers

**ANS Physiology:**

**Neuroeffector Junction of ANS:**

- Postganglionic neuron forms diffuse, branching networks at synapse
  - NTs released from varicosities ("beads")
  - Innervation by multiple ANS fibers may occur
  - Postsynaptic receptors spread across target

**Precision strike** vs. **Saturation bombing**

**Remember:**

- Neuromuscular junction
Fiber Types:

- Cholinergic Fibers: Synthesize / secrete acetylcholine (NT)
  - All preganglionic fibers (sympathetic and parasympathetic divisions)
  - Postganglionic fibers of parasympathetic division
- Adrenergic Fibers: Synthesize / secrete norepinephrine (NT)
  - Postganglionic fibers of sympathetic division (sans sweat glands / piloerector muscles)

Synthesis of Neurotransmitters:

- NTs synthesized / stored in varicosities of nerve fibers

<table>
<thead>
<tr>
<th>Acetyl-CoA + Choline</th>
<th>Tyrosine</th>
</tr>
</thead>
<tbody>
<tr>
<td>choline acetetyltransferase</td>
<td>hydroxylation</td>
</tr>
<tr>
<td></td>
<td>Dopa</td>
</tr>
<tr>
<td></td>
<td>decarboxylation</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>Dopamine</td>
</tr>
<tr>
<td></td>
<td>hydroxylation</td>
</tr>
<tr>
<td>Choline recycled...</td>
<td>Norepinephrine</td>
</tr>
</tbody>
</table>

Removal:

1) Reuptake (~ 80%)
2) Diffusion (~ 20%)
3) Destruction (> 1%)

ANS Physiology:

Receptor Types:

A) Adrenoreceptors (bind E / NE):
  - Located on target tissues of sympathetic nervous system
ANS Physiology:
G – protein Receptor Systems:
- Receptors interact with G-proteins to trigger cellular event

A. Receptors:
- 7 trans-membrane segments (each segment = similar α-helix sequences)
- Interact with various G-proteins depending on sequence of 3rd intracellular loop

B. G proteins:
- Composed of three unique sub-units (α, β, δ)
- No intrinsic enzymatic activity; activates enzymes

G protein Activation:
1) Ligand binds to receptor
2) Receptor / G protein interact
   - GDP (α-subunit) replaced by GTP; dissociation occurs
3) α-subunit activates effector
   - Hydrolysis of GTP to GDP causes α-subunit to dissociate from effector and rejoin other subunits
ANS Physiology:
G – protein Receptor Systems:
  • Receptors interact with G-proteins to trigger cellular event

C. Effectors:
  A) **Adenylate cyclase** (*2nd* messenger – cAMP)
    - Synthesizes cAMP from ATP
    - Methylxanthines (e.g., caffeine)
        - Inactivates cAMP
ANS Physiology:

G – protein Receptor Systems:
• Receptors interact with G-proteins to trigger cellular event

C. Effectors:
A) Adenylate cyclase (2nd messenger – cAMP)
B) Phospholipase C (2nd messengers – IP₃ / DAG)
  • IP₃ activates release of Ca²⁺ (ER)
  • DAG activates protein kinase

Phosphoinositol (PIP)
Diacylglycerol (DAG)
Inositol triphosphate (IP₃)

Wolfe – Figure 6.6 / 6.9

ANS Physiology:

Receptor Types:

A) Adrenoreceptors (bind E / NE):
  • Located on target tissues of sympathetic NS
  • Divided into two types: α and β receptors

<table>
<thead>
<tr>
<th>Receptor Type</th>
<th>Effect</th>
<th>Location</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>α₁ receptors</td>
<td>(+) Excitatory (+)</td>
<td>Vascular smooth muscle - skin (constricts blood vessels)</td>
<td>G protein coupled to phosphorylase C</td>
</tr>
<tr>
<td>α₂ receptors</td>
<td>(-) Inhibitory (-)</td>
<td>Membrane of adrenergic axon terminals (inhibits NE release)</td>
<td>G protein coupled to adenylate cyclase</td>
</tr>
</tbody>
</table>

Nature of receptor dictates effects of NTs

Phenylephrine (α₁ agonist)
ANS Physiology:
Receptor Types:

A) **Adrenoreceptors** (bind E / NE):
- Located on target tissues of sympathetic NS
- Divided into two types: α and β receptors

<table>
<thead>
<tr>
<th>β₁ receptors</th>
<th>β₂ receptors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effect:</strong> (+) Excitatory (+)</td>
<td><strong>Effect:</strong> (-) Inhibitory (-)</td>
</tr>
<tr>
<td><strong>Location:</strong> Predominately in the heart (increases contraction rate / strength)</td>
<td><strong>Location:</strong> Vascular smooth muscle - skeletal muscle (dilates vessels)</td>
</tr>
<tr>
<td>Kidney (triggers renin (hormone) release)</td>
<td>Lungs (dilates bronchioles)</td>
</tr>
<tr>
<td><strong>Mechanism of Action:</strong> Gs protein coupled to adenylate cyclase</td>
<td><strong>Mechanism of Action:</strong> Gs protein coupled to adenylate cyclase</td>
</tr>
</tbody>
</table>

- **Propanolol** (β-blocker)
- **Albuterol** (β₂ agonist)

B) **Cholinoreceptors** (bind ACh):
- Located on postganglionic neurons / target tissues of parasympathetic NS
- Divided into two types: nicotinic & muscarinic

<table>
<thead>
<tr>
<th>Nicotinic</th>
<th>Muscarinic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effect:</strong> (+) Excitatory (+)</td>
<td><strong>Effect:</strong> (+) Excitatory (+) &amp; (-) Inhibitory (-)</td>
</tr>
<tr>
<td><strong>Location:</strong> Motor end plate – skeletal muscle (contracts skeletal muscle)</td>
<td><strong>Location:</strong> Parasympathetic organs – sans heart (excites organ activity)</td>
</tr>
<tr>
<td>All postganglionic neurons (activate postganglionic neurons)</td>
<td></td>
</tr>
<tr>
<td>Chromaffin cells – adrenal medulla (triggers release of E / NE)</td>
<td><strong>Sweat glands – sympathetic NS</strong> (activates sweat glands)</td>
</tr>
<tr>
<td><strong>Mechanism of Action:</strong> Ligand-gated ion channel</td>
<td><strong>Mechanism of Action:</strong> G protein coupled to phosphorylase C (Majority of locations)</td>
</tr>
</tbody>
</table>

**Atropine** (muscarinic antagonist)
Autonomic Nervous System

ANS Physiology:

Parasympathetic

Muscarinic receptors

Visceral effector cell

Cholinergic fibers

Nicotinic receptors

Autonomic ganglion

Visceral effector cell

Sympathetic

Adrenergic fibers

Adrenergic receptors (α/β)

Autonomic ganglion

Costanzo – Figure 2.1

Autonomic Nervous System

ANS Physiology:

CENTRAL NERVOUS SYSTEM

Somatic

Motor neuron

Preganglionic

Postganglionic

ACH

NE

Skeletal muscle

Smooth muscle, glands

Sweat glands*

Smooth muscle, glands

Parasympathetic

Preganglionic

Postganglionic

ACH

NE

Costanzo – Figure 2.1
ANS Physiology:
Control of Autonomic Functioning:

A) Brain stem / Spinal cord
- Vasomotor center (cardiovascular)
- Respiratory center
- Micturition center (urination)
- Swallowing / coughing / vomiting

B) Hypothalamus
- Main integration center
  - Body temperature
  - Water balance
  - Food intake
- Links emotion with ANS

C) Cortical control
- Links emotional past with ANS
- Voluntary cortical ANS control possible

Interactions of Autonomic Divisions:

A) Antagonistic Interactions:
- Pupil:
  - Parasympathetic = Constriction (circular fibers)
  - Sympathetic = Dilation (meridional fibers)
- Heart (sinoatrial node):
  - Parasympathetic = Decrease heart rate
  - Sympathetic = Increase heart rate

B) Synergistic Interactions:
- External genitalia
  - Parasympathetic = Vasodilation of blood vessels (erection of tissue)
  - Sympathetic = Smooth muscle contraction (ejaculation / reflex contraction)

* Tone:
- Basal rate of activity present in a system
- Allows increase / decrease by single system

Blood vessels under sympathetic tone
Decrease output = vasodilation of vessel
Increase output = vasoconstriction of vessel
ANS Physiology:

Interactions of Autonomic Divisions:

C) Coordinated Function within Organ:

- **Sympathetic**
  - Bladder:
    - Filling = *Relaxed* detrusor muscle; *contracted* internal sphincter
    - Emptying = *Contracted* detrusor muscle; *relaxed* internal sphincter

- **Parasympathetic**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Filling of Bladder</th>
<th>Control Mechanism</th>
<th>Emptying of Bladder</th>
<th>Control Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detrusor muscle</td>
<td>Relaxed</td>
<td>Sympathetic</td>
<td>Contracted</td>
<td>Parasympathetic</td>
</tr>
<tr>
<td>Internal sphincter</td>
<td>Contracted</td>
<td>Sympathetic</td>
<td>Relaxed</td>
<td>Parasympathetic</td>
</tr>
<tr>
<td>External sphincter</td>
<td>Contracted</td>
<td>Voluntary</td>
<td>Relaxed</td>
<td>Voluntary</td>
</tr>
</tbody>
</table>

Adrenal Medulla:

- Large sympathetic ganglion
- Postganglionic cells = Chromaffin cells
- Releases **catecholamines** (epinephrine (80%) and norepinephrine (20%))
- Catecholamines transported via blood (= hormone)
  - Delayed effect (3 – 5 sec.); prolonged effect (2 – 4 min. to clear from system)
    - Stimulation of cardiovascular function / metabolic rate (helps deal with stress)
- Perceived purpose:
  1) Safety factor (dual mechanism – backs up sympathetic nervous system)
  2) Stimulate structures not directly innervated (e.g., every cell of body…)