AUTONOMIC NEUROCHEMISTRY

Autonomic Neurochemistry

Last updated: April 20, 2019

**TRANSMITTERS**

1. **ACETYLCHOLINE**:  
   1) all *preganglionic* neurons  
   2) anatomically *parasympathetic postganglionic* neurons  
   3) anatomically *sympathetic postganglionic* neurons which innervate:  
      - sweat glands  
      - *blood vessels in skeletal muscles* and produce vasodilation when stimulated  
      (sympathetic vasodilator nerves)  
   - no acetylcholine exists in circulating blood - effects of cholinergic discharge are localized, discrete and of short duration (high concentration of acetylcholinesterase at cholinergic nerve endings).

2. **NOREPINEPHRINE** - most *postganglionic sympathetic* neurons.  
   - spreads farther and has more prolonged action than acetylcholine.  
   - norepinephrine, epinephrine, dopamine are all found in plasma (epinephrine and dopamine come from adrenal medulla, vs. most of norepinephrine - from noradrenergic endings).

- **DOPAMINE** - secreted by *interneurons in sympathetic ganglia*.  
- **GnRH** - secreted by some of *preganglionic neurons*.  
- **ADRENAL MEDULLA** is essentially sympathetic ganglion in which postganglionic cells have lost their axons and secrete norepinephrine, epinephrine, and some dopamine directly into bloodstream.

- **cotransmitters**:
  1) **VIP** - released with *acetylcholine*;  
     - *vasodilation* (blood flow↑ into target organ).  
     - *bronchodilation* (there may be separate **VIP-SECRETING NERVOUS SYSTEM** innervating bronchial smooth muscle).  
  2) **ATP** and **neuropeptide Y** - released with **norepinephrine**.

**RESPONSES**

<table>
<thead>
<tr>
<th>Effector organ</th>
<th>Cholinergic impulse</th>
<th>Noradrenergic impulse</th>
<th>receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EYE</strong></td>
<td>Iris (radial muscle)</td>
<td>–</td>
<td>contraction (mydriasis)</td>
</tr>
<tr>
<td>Iris (sphincter muscle)</td>
<td>contraction (miosis)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td><strong>Ciliary muscle</strong></td>
<td>contraction (for near vision)</td>
<td>relaxation (for far vision)</td>
<td>$\beta_2$</td>
</tr>
<tr>
<td><strong>HEART</strong></td>
<td>SA node</td>
<td>heart rate↓ (vagal arrest)</td>
<td>heart rate↑</td>
</tr>
<tr>
<td>Organ System</td>
<td>Effect in Positive</td>
<td>Effect in Negative</td>
<td></td>
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<td>-----------------------</td>
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</tr>
<tr>
<td><strong>Atria</strong></td>
<td>contractility↓, conduction velocity↑</td>
<td>contractility↑, conduction velocity↑</td>
<td></td>
</tr>
<tr>
<td><strong>AV node, His-Purkinje system</strong></td>
<td>conduction velocity↓</td>
<td>conduction velocity↑, refractory period↓</td>
<td></td>
</tr>
<tr>
<td><strong>Ventricles</strong></td>
<td>contractility↓</td>
<td>contractility↑</td>
<td></td>
</tr>
<tr>
<td><strong>Coronary</strong></td>
<td>constriction</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Skin &amp; mucosa, salivary glands</strong></td>
<td>dilation</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Cerebral</strong></td>
<td>dilation</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Skeletal muscle, pulmonary</strong></td>
<td>dilation</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Abdominal viscera</strong></td>
<td>–</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>–</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Systemic Veins</strong></td>
<td>–</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Bronchi</strong></td>
<td>muscle contraction</td>
<td>relaxation</td>
<td></td>
</tr>
<tr>
<td><strong>Glands</strong></td>
<td>stimulation</td>
<td>inhibition</td>
<td></td>
</tr>
<tr>
<td><strong>Tone &amp; Motility</strong></td>
<td>increase</td>
<td>decrease</td>
<td></td>
</tr>
<tr>
<td><strong>Sphincters</strong></td>
<td>relaxation</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Secretion</strong></td>
<td>stimulation</td>
<td>inhibition</td>
<td></td>
</tr>
<tr>
<td><strong>Gallbladder, bile ducts</strong></td>
<td>contraction</td>
<td>relaxation</td>
<td></td>
</tr>
<tr>
<td><strong>Juxtaglomerular cells</strong></td>
<td>–</td>
<td>renin secretion</td>
<td></td>
</tr>
<tr>
<td><strong>Ureters</strong></td>
<td>motility &amp; tone</td>
<td>increase</td>
<td></td>
</tr>
<tr>
<td><strong>Urinary bladder</strong></td>
<td>detrusor contraction</td>
<td>relaxation</td>
<td></td>
</tr>
<tr>
<td><strong>Trigone &amp; sphincter</strong></td>
<td>relaxation</td>
<td>constriction</td>
<td></td>
</tr>
<tr>
<td><strong>Uterus</strong></td>
<td>variable (depends on menstrual cycle stage, circulating estrogen and progesterone, pregnancy, etc)</td>
<td>contraction (pregnant)</td>
<td></td>
</tr>
<tr>
<td><strong>Male sex organs</strong></td>
<td>erection</td>
<td>ejaculation</td>
<td></td>
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<tr>
<td><strong>Skin</strong></td>
<td>sweat glands</td>
<td>slight, localized secretion (on palms – “adrenergic sweating”)</td>
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<tr>
<td><strong>Pilomotor muscles</strong></td>
<td>–</td>
<td>contraction</td>
<td></td>
</tr>
<tr>
<td><strong>Spleen capsule</strong></td>
<td>–</td>
<td>contraction</td>
<td></td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td>–</td>
<td>relaxation</td>
<td></td>
</tr>
<tr>
<td><strong>Adrenal medulla</strong></td>
<td>NA &amp; A secretion</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td><strong>Skeletal muscle</strong></td>
<td>contraction</td>
<td>glycogenolysis, tremor</td>
<td></td>
</tr>
<tr>
<td><strong>Adipose tissue</strong></td>
<td>–</td>
<td>lipolysis</td>
<td></td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td>exocrine secretion↑</td>
<td>secretion↓</td>
<td></td>
</tr>
<tr>
<td><strong>Endocrine (insulin &amp; glucagon secretion)</strong></td>
<td>secretion↑</td>
<td>secretion↓</td>
<td></td>
</tr>
<tr>
<td><strong>Salivary glands</strong></td>
<td>secretion↑ (profuse, watery)</td>
<td>secretion↑ (thick, viscous)</td>
<td></td>
</tr>
</tbody>
</table>
A

AUTONOMIC NEUROCHEMISTRY

<table>
<thead>
<tr>
<th></th>
<th>amylase secretion</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>NASOPHARYNGEAL GLANDS</td>
<td>secretion↑</td>
<td>–</td>
</tr>
<tr>
<td>LACRIMAL GLANDS</td>
<td>secretion↑</td>
<td>secretion↑</td>
</tr>
<tr>
<td>PINEAL GLAND</td>
<td>–</td>
<td>melatonin synthesis &amp; secretion</td>
</tr>
</tbody>
</table>

cardiovascular effects – also see 1276, 1319 p. (CARDIOVASCULAR)

**RECEPTOR TYPES**

- N cholinoreceptors – coupled to ion channels
- M cholinoreceptors – coupled to Gq proteins (IP3 & DAG↑), except M2 - Gi
- α1 adrenoreceptors – coupled to Gq proteins (IP3 & DAG↑)
- α2 adrenoreceptors – coupled to Gi proteins (cAMP↓)
- β1, β2 adrenoreceptors – coupled to Gs proteins (cAMP↑).

**CHOLINERGIC division** is concerned with vegetative aspects of day-to-day living – “rest and digest”.

N.B. parasympathetic system never discharges diffusely (if it did → massive, undesirable, unpleasant symptoms) – actions are discrete & localized; parasympathetic system maintains bodily functions essential for life!

**NORADRENERGIC division** discharges as unit (together with adrenal medulla) in emergency situations (e.g. trauma, fear, hypoglycemia, cold, exercise) - "fright → flight or fight":

- 1) dilates pupils (letting more light into eyes)
- 2) accelerates heartbeat and raises BP (providing better perfusion of vital organs and muscles)
- 3) bronchodilates
- 4) constricts skin blood vessels (limits bleeding from wounds).
- 5) lowers thresholds in reticular formation (reinforcing alert, aroused state)
- 6) elevates plasma glucose and free fatty acid levels (supplying more energy).

- other noradrenergic actions also exists, e.g. continuous tonic noradrenergic discharge to arterioles maintains arterial pressure (in fasting sympathetic tonus↓ → decrease in blood pressure and metabolic rate).

N.B. sympathetic system discharges as unit and diffusely; sympathetic system is not essential for life!

- smooth muscle in hollow viscera walls is innervated by both noradrenergic and cholinergic fibers (activity in one system increases intrinsic activity of smooth muscle whereas activity in other decreases it); however, there is no uniform rule about which system stimulates and which inhibits.
- in sphincter muscles, both noradrenergic and cholinergic innervations are excitatory, but one supplies constrictor component and other dilator.

**MODES OF TRANSMISSION**

1. Ganglionic transmission

- acetylcholine acting on N cholinergic receptors see A4b p.

N.B. N cholinoreceptors in ganglia are slightly different from N cholinoreceptors in neuromuscular junction; main differences:

- single preganglionic fiber does not release enough transmitter to depolarize postganglionic neuron to threshold – summation is necessary (vs. somatic motoneurons always activate muscle fibers)
- receptors are blocked by different drugs:
in neuromuscular junction – by *curare-type drugs*;
in ganglia – by *ganglionic blockers*.

Responses of **postganglionic sympathetic** neurons:

<table>
<thead>
<tr>
<th>Potential</th>
<th>Duration</th>
<th>Transmitter</th>
<th>Receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast EPSP</td>
<td>30 ms</td>
<td>Acetylcholine</td>
<td>N</td>
</tr>
<tr>
<td>Slow IPSP</td>
<td>2 sec</td>
<td>Dopamine (secreted by interneurons within ganglion – so called SIF [small - intensely fluorescent] cells)</td>
<td>D2</td>
</tr>
<tr>
<td>Slow EPSP</td>
<td>30 sec</td>
<td>Acetylcholine</td>
<td>M2</td>
</tr>
<tr>
<td>Late slow EPSP</td>
<td>4 min</td>
<td>GnRH</td>
<td>GnRH</td>
</tr>
</tbody>
</table>

EPSP - excitatory postsynaptic potential
IPSP - inhibitory postsynaptic potential

- **fast EPSP** - generates action potential.
- **prolonged potentials** (slow IPSP, slow EPSP, late slow EPSP) - modulate transmission through sympathetic ganglia.

2. Postganglionic PARASYMPATHETIC transmission

- acetylcholine acting on **M cholinergic receptors** see A4b p.

**Excitatory effects** – on smooth muscles (GI & GU tracts [except sphincters], bronchi), glands.

**Inhibitory effects** – on heart (pacemaker activity↓ in SA node, conduction↓ in AV node).

3. Postganglionic SYMPATHETIC transmission

- norepinephrine acting on **α and β adrenergic receptors** see A4b p.

- **receptor location/action:**
  - α1 – vazokonstrikcija (AKS↑), midriasis, gimdos kontrakcija, šl.pūslės sfinkterio kontrakcija.
  - α2 – presinaptinė NA sekrecijos inhibicija, insulino sekrecijos inhibicija, trombocitų agregacija.
  - β1 – kardiostimuliacija, lipolizė, renino sekrecija.
  - β2 – vazodilatacija, bronchodilatacija, GI traktos inhibicija, gimdos relaksacija, gliukagono sekrecija & glikogenolizė.

- **α receptors** (sensitive to both NA and A);
  - α1 receptors produce mainly **Excitatory effects** (+ at least one Inhibitory – intestinal motility inhibition);
  - α2 receptors produce mainly **Inhibitory effects** (except in blood vessels)

N.B. α2 receptors also may be **presynaptic** – inhibit further NA release.

- **β receptors** (sensitive to A but relatively insensitive to NA) produce mainly **Inhibitory effects** (+ at least one excitatory – heart stimulation).

- **effects of adrenomedullary** stimulation (epinephrine, A) and **sympathetic nerve** stimulation (norepinephrine, NA) generally are similar; however, in some tissues, A and NA produce different effects – due to predominance of different receptors (α / β)
  - e.g. β2 receptors predominate in coronary & skeletal muscle arterioles (→ vasodilation), vs. in other arterioles α1 receptors predominate (→ vasoconstriction); heart contains predominantly β1 receptors.
BIBLIOGRAPHY for ch. “Autonomic PNS” → follow this LINK >>
Ganong “Review of Medical Physiology”, 2002