Autonomic Neurochemistry

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Transmitters

1. **Acetylcholine**:
2. all ***preganglionic*** neurons
3. anatomically ***parasympathetic postganglionic*** neurons
4. 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).
5. **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).

1. **ATP** and **neuropeptide Y** - released with ***norepinephrine***.

Responses

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Effector organ | | **Cholinergic** impulse | **Noradrenergic** impulse | |
| response | receptor |
| Eye | **Iris** (radial muscle) | – | contraction (mydriasis) | α1 |
| **Iris** (sphincter muscle) | contraction (miosis) | – | |
| **Ciliary** muscle | contraction (for near vision) | relaxation (for far vision) | β2 |
| Heart | SA node | heart rate↓ (vagal arrest) | heart rate↑ | β1 |
| atria | contractility↓, conduction velocity↑ | contractility↑, conduction velocity↑ |
| **AV node**,  **His-Purkinje system** | conduction velocity↓ | conduction velocity↑, refractory period↓ |
| ventricles | contractility↓ | contractility↑ |
| Arterioles | coronary | constriction | constriction | α1, α2 |
| dilation | β2 |
| skin & mucosa, salivary glands | dilation | constriction | α1, α2 |
| **cerebral** | dilation | constriction | α1 |
| **skeletal muscle, pulmonary** | dilation | constriction | α1 |
| dilation | β2 |
| **abdominal viscera** | – | constriction | α1 |
| dilation | β2 |
| **renal** | – | constriction | α1, α2 |
| dilation | β1, β2 |
| Systemic Veins | | – | constriction | α1, α2 |
| dilation | β2 |
| Bronchi | **muscle** | contraction | relaxation | β2 |
| **glands** | stimulation | inhibition | α1 |
| stimulation | β2 |
| Stomach,  Intestine | **tone & motility** | increase | decrease | α1, α2, β1, β2 |
| **sphincters** | relaxation | contraction | α1 |
| **secretion** | stimulation | inhibition | α2 |
| Gallbladder, bile ducts | | contraction | relaxation | β2 |
| Juxtaglomerular cells | | – | renin secretion | β1 |
| Ureters **motility & tone** | | increase (?) | increase | α1 |
| Urinary bladder | **detrusor** | contraction | relaxation | β2 |
| **trigone & sphincter** | relaxation | contraction | α1 |
| Uterus | | variable (depends on menstrual cycle stage, circulating estrogen and progesterone, pregnancy, etc) | contraction (pregnant) | α1 |
| relaxation | β2 |
| Male sex organs | | erection | ejaculation | α1 |
| Skin | **sweat glands** | generalized secretion | slight, localized secretion (on palms – “adrenergic sweating”) | α1 |
| **pilomotor muscles** | – | contraction | α1 |
| Spleen capsule | | – | contraction | α1 |
| relaxation | β2 |
| Adrenal medulla | | NA & A secretion | – | |
| Liver | | – | glycogenolysis | α1, β2 |
| Skeletal muscle | | contraction | glycogenolysis, tremor | β |
| Adipose tissue | | – | lipolysis | α1, β1, β3 |
| Pancreas | **exocrine** | secretion↑ | secretion↓ | α |
| **endocrine** (insulin & glucagon secretion) | secretion↑ | secretion↓ | α2 |
| secretion↑ | β2 |
| Salivary glands | | secretion↑ (profuse, watery) | secretion↑ (thick, viscous) | α1 |
| amylase secretion | β |
| Nasopharyngeal glands | | secretion↑ | – | |
| Lacrimal glands | | secretion↑ | secretion↑ | α |
| Pineal gland | | – | melatonin synthesis & secretion | β |

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:

|  |  |  |  |
| --- | --- | --- | --- |
| **Potential** | **Duration** | **Transmitter** | **Receptor** |
| **Fast EPSP** | 30 ms | **Acetylcholine** | N |
| **Slow IPSP** | 2 sec | **Dopamine** (secreted by interneurons within ganglion – so called **SIF [small - intensely fluorescent] cells**) | D2 |
| **Slow EPSP** | 30 sec | **Acetylcholine** | M2 |
| **Late slow EPSP** | 4 min | **GnRH** | GnRH |

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.

1. 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).

1. 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 trakto 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)

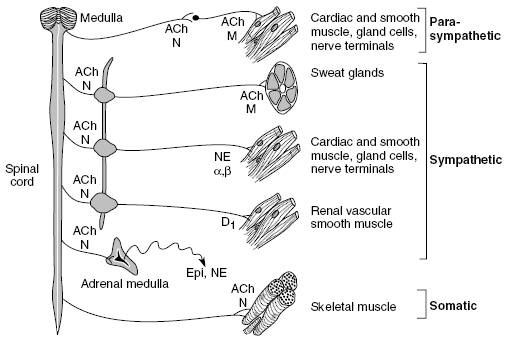
N.B. **α2 receptors** also may be **presynaptic** – inhibit further NA release.

**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 >>](http://www.neurosurgeryresident.net/A.%20Neuroscience%20Basics\A.%20Bibliography.pdf)

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Lippincott’s Pharmacology Review, 2nd ed., 2000

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