Autonomic Neurochemistry

Last updated: September 5, 2017

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

Effector organ		**Cholinergic** impulse	**Noradrenergic** impulse	
			response	receptor
EYE	**Iris** (radial muscle)	–	contraction (mydriasis)	α_1
	Iris (sphincter muscle)	contraction (miosis)	–	
	Ciliary muscle	contraction (for near vision)	relaxation (for far vision)	β_2
HEART	**SA node**	heart rate↓ (vagal arrest)	heart rate↑	β_1

	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	α_1, α_2
			dilation	β_2
	skin & mucosa, salivary glands	dilation	constriction	α_1, α_2
	cerebral	dilation	constriction	α_1
	skeletal muscle, pulmonary	dilation	constriction	α_1
			dilation	β_2
	abdominal viscera	–	constriction	α_1
			dilation	β_2
	renal	–	constriction	α_1, α_2
			dilation	β_1, β_2
SYSTEMIC VEINS		–	constriction	α_1, α_2
			dilation	β_2
BRONCHI	**muscle**	contraction	relaxation	β_2
	glands	stimulation	inhibition	α_1
			stimulation	β_2
STOMACH, INTESTINE	**tone & motility**	increase	decrease	α_1, α_2, β_1, β_2
	sphincters	relaxation	contraction	α_1
	secretion	stimulation	inhibition	α_2
GALLBLADDER, BILE DUCTS		contraction	relaxation	β_2
JUXTAGLOMERULAR CELLS		–	renin secretion	β_1
URETERS	**motility & tone**	increase (?)	increase	α_1
URINARY BLADDER	**detrusor**	contraction	relaxation	β_2
	trigone & sphincter	relaxation	contraction	α_1
UTERUS		variable (depends on menstrual cycle stage, circulating estrogen and progesterone, pregnancy, etc)	contraction (pregnant)	α_1
			relaxation	β_2
MALE SEX ORGANS		erection	ejaculation	α_1
SKIN	**sweat glands**	generalized secretion	slight, localized secretion (on palms – "adrenergic sweating")	α_1
	pilomotor muscles	–	contraction	α_1
SPLEEN CAPSULE		–	contraction	α_1
			relaxation	β_2
ADRENAL MEDULLA		NA & A secretion	–	
LIVER		–	glycogenolysis	α_1, β_2
SKELETAL MUSCLE		contraction	glycogenolysis, tremor	β
ADIPOSE TISSUE		–	lipolysis	α_1, β_1, β_3
PANCREAS	**exocrine**	secretion↑	secretion↓	α
	endocrine (insulin & glucagon secretion)	secretion↑	secretion↓	α_2
			secretion↑	β_2
SALIVARY GLANDS		secretion↑ (profuse, watery)	secretion↑ (thick, viscous)	α_1

		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 G_q proteins (IP_3 & DAG↑), except M_2 - G_i
α_1 adrenoreceptors – coupled to G_q proteins (IP_3 & DAG↑)
α_2 adrenoreceptors – coupled to G_i proteins (cAMP↓)
β_1, β_2 adrenoreceptors – coupled to G_s 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**)	D_2
Slow EPSP	30 sec	**Acetylcholine**	M_2
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.

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

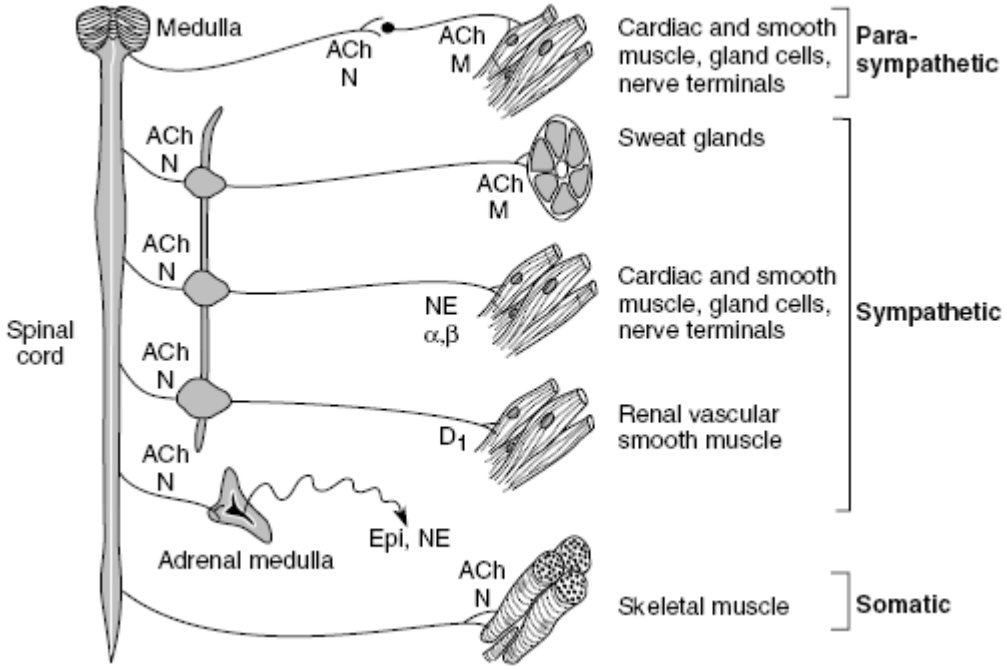
- **norepinephrine** acting on **α and β adrenergic receptors** see A4b p.

- receptor location/action:
  α_1 – vazokonstrikcija (AKS↑), midriasis, gimdos kontrakcija, šl.pūslės sfinkterio kontrakcija.
  α_2 – presinaptinė NA sekrecijos inhibicija, insulino sekrecijos inhibicija, trombocitų agregacija.
  β_1 – kardiostimuliacija, lipolizė, renino sekrecija.
  β_2 – vazodilatacija, bronchodilatacija, GI trakto inhibicija, gimdos relaksacija, gliukagono sekrecija & glikogenolizė.

- **α receptors** (sensitive to both NA and A);
  α_1 receptors produce mainly EXCITATORY effects (+ at least one INHIBITORY – intestinal motility inhibition);
  α_2 receptors produce mainly INHIBITORY effects (except in blood vessels)
  N.B. **α_2 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. **β_2** receptors predominate in *coronary & skeletal muscle arterioles* (→ vasodilation), vs. in *other arterioles* **α_1** receptors predominate (→ vasoconstriction); *heart* contains predominantly **β_1** receptors.



BIBLIOGRAPHY for ch. "Autonomic PNS" → follow this LINK >>
Ganong "Review of Medical Physiology", 2002
Lippincott's Pharmacology Review, 2nd ed., 2000