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Lecture title: Sympathetic and Parasympathetic Neurons Secretion

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Summary:

Most Sympathetic and Parasympathetic Neurons Secrete Either Acetylcholine or Norepinephrine as a Neurotransmitter

*Acetylcholine is the neurotransmitter at the somatic neuromuscular synapse. Acetylcholine is also released by the preganglionic neurons at all autonomic ganglia. *Parasympathetic postganglionic neurons release acetylcholine as well, onto their target organs. Acetylcholinereleasing synapses are often called cholinergic. Most anatomically sympathetic postganglionic neurons secrete norepinephrine onto their targets. Norepinephrine-releasing synapses are often called adrenergic.

*However, in several species, anatomically sympathetic postganglionic neurons traveling to sweat glands secrete acetylcholine, as do some of the sympathetic postganglionic neurons to blood vessels in skeletal muscle, where they can produce vasodilation.

*In the case of the adrenal medulla, incoming preganglionic axons release acetylcholine, but the neuroendocrine-like, postganglionic chromaffin cells release primarily epinephrine and some norepinephrine into the circulating blood. These chromaffin cells can be considered structural and functional analogues of sympathetic postganglionic neurons. It is important that, when released, the neurotransmitter not linger in the synaptic cleft.

*The neurotransmitter must be either destroyed in the cleft or dissipated so that the postsynaptic membrane can recover its resting potential and be ready for the next synaptic transmission. Because some synapses can transmit impulses up to several hundred times per second, neurotransmitter destruction must occur quickly. In the case of acetylcholine, acetylcholinesterase destroys the transmitter in the cleft. For norepinephrine, reuptake by the presynaptic neuron is the principal way in which its synaptic effect on the postsynaptic membrane is terminated.

*The hormonal actions of circulating epinephrine and norepinephrine released by the adrenal medulla, however, are primarily terminated by the enzyme catechol-O-methyltransferase (COMT), with a lesser contribution of the enzyme monoamine oxidase (MAO). These enzymes are widely distributed in the body, with highest concentrations in the liver and kidney.

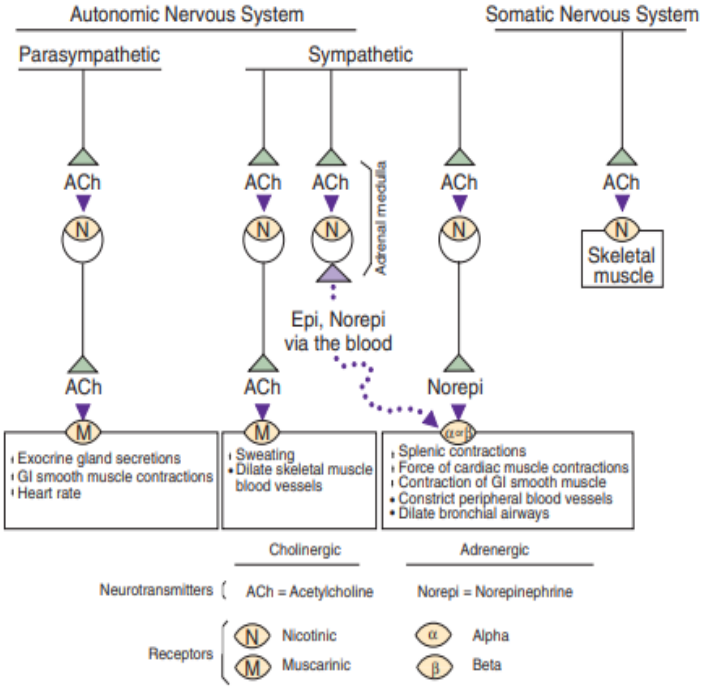

FIGURE 13-4 Classification of autonomic and somatic motor neurons with regard to their transmitter or mediator released, their postsynaptic receptors, and their general influence on the effector organ. Acetylcholine *(ACh)*, released from the presynaptic membrane, can stimulate either a muscarinic *(M)* or a nicotinic *(N)* postsynaptic receptor, depending on the particular location of the synapse. Similarly, norepinephrine *(Norepi)* can stimulate either α or β receptors, again depending on the location of the synapse. *Epi*, Epinephrine; *GI*, gastrointestinal.

Acetylcholine and Norepinephrine Have Different Postsynaptic Receptors

*The neurotransmitters secreted by the ANS typically stimulate their target organ by first binding with a postsynaptic receptor. These receptors are proteins in the cell membrane. When the transmitter binds with the postsynaptic receptor, the membrane's

permeability to selected ions is often changed, and the postsynaptic membrane potential either increases or decreases, with a resulting change in the probability of action potentials in the postsynaptic cell.

*Acetylcholine stimulates two different types of receptors. Muscarinic acetylcholine receptors are G-protein–coupled receptors found on all the target cells stimulated by postganglionic parasympathetic neurons and by cholinergic postganglionic neurons of the sympathetic nervous system.

*Faster acting nicotinic receptors are ligand-gated ion channels found at all synapses between autonomic preganglionic and postganglionic neurons and at the somatic neuromuscular junction.

*The classification of major types and subtypes of neurotransmitter receptors is usually based upon various combinations of the following: responses to agonist or antagonist drugs, distribution among various tissues and organs, signal transduction mechanism (e.g., G protein-coupled, ligand-gated).

*Muscarinic receptors were named because they are stimulated by muscarine, a toadstool poison.

*Muscarine does not stimulate nicotinic receptors.

*Nicotine stimulates the nicotinic receptors but not muscarinic receptors. *Acetylcholine stimulates both, and different drugs block each receptor. For example, atropine blocks muscarinic receptors, whereas curare blocks nicotinic receptors. *Although there are respective subtypes of nicotinic (e.g., Nm, Nn) and muscarinic (e.g., M1-M5) acetylcholine receptors, there are few therapeutic drugs that can distinguish among subtype members.

*Adrenergic receptors are located at synapses between peripheral target tissues and sympathetic postganglionic neurons that release norepinephrine.

*However, these receptors can also be stimulated by the release of epinephrine and norepinephrine into the bloodstream from the adrenal medulla. There are two major types of adrenergic receptors, called alpha (α) and beta (β) receptors. The β receptors have been further subdivided into β1 and β2 receptors, on the basis of the effect of adrenergic blocking and stimulating drugs. There is now evidence for a third class of βreceptor (β3, found in fat cells), and for two classes of α receptors (α1 and α2) that can each be divided into additional subtypes. All adrenergic receptors are GPCRs, and the various subtypes, like the cholinergic receptor subtypes, have differential distributions among various tissues. There are many clinically useful drugs that can distinguish among the members within adrenergic receptor subtype groups.

Table 2-2 Prototypes of Agonists and Antagonists to Autonomic Receptors

Receptor	Agonists	Antagonists
Adrenoreceptors		
α_1	Norepinephrine Phenylephrine	Phenoxybenzamine Prazosin
α_2	Clonidine	Yohimbine
β_1	Norepinephrine Isoproterenol	Propranolol Metoprolol
β_2	Epinephrine Isoproterenol Albuterol	Propranolol Butoxamine
Cholinoreceptors		
Nicotinic	Ach Nicotine Carbachol	Curare Hexamethonium (blocks ganglionic receptor but not neuromuscular junction)
Muscarinic	Ach Muscarine Carbachol	Atropine

ACh, Acetylcholine.

Table 2-4 Location and Mechanism of Action of Autonomic Receptors

Receptor	Target Tissue	Mechanism of Action
Adrenoreceptors		
α_1	Vascular smooth muscle, skin, renal, and splanchnic Gastrointestinal tract, sphincters Bladder, sphincter Radial muscle, iris	IP_3, ↑ intracellular $[Ca^{2+}]$
α_2	Gastrointestinal tract, wall Presynaptic adrenergic neurons	Inhibition of adenylyl cyclase, ↓ cAMP
β_1	Heart Salivary glands Adipose tissue Kidney	Stimulation of adenylyl cyclase, ↑ cAMP
β_2	Vascular smooth muscle of skeletal muscle Gastrointestinal tract, wall Bladder, wall Bronchioles	Stimulation of adenylyl cyclase, ↑ cAMP
Cholinoreceptors		
Nicotinic	Skeletal muscle, motor end plate Postganglionic neurons, SNS and PNS Adrenal medulla	Opening Na^+ and K^+ channels → depolarization
Muscarinic	All effector organs, PNS Sweat glands, SNS	IP_3, ↑ intracellular $[Ca^{2+}]$

cAMP, Cyclic adenosine monophosphate; PNS, parasympathetic nervous system; SNS, sympathetic nervous system.