

Muscarinic ACh receptors (mAChRs) Location

Muscarinic 1 (M1)	Ganglia cells
Muscarinic 2 (M2)	Cardiac muscle
Muscarinic 3 (M3)	Sweat glands
Muscarinic 4 & 5 (M4 & M5) are NOT very important in this module.	

Muscarinic Effects on Organ

Heart	↓ HR	M2
Eye (circular musc.)	Pinpoint pupil	M2 & M3
Eye (ciliary musc.)	Contract	M3
Vascular musc.	Relax	M3 (NO)
Lungs (Broncho musc.)	Contract	M3
GI-tract	↑ motility	M3
Genito-urinary musc.	Contract	M3
Sweat & Salivary Gland	↑ excretion	M3

Parasympathetic Agonist Effects

Heart	↓ CO = ↓ contraction & ↓ AV conduction speed = BRADYcardia
Vascular musc.	Vasodilation via (NO) production
Smooth musc.	↑ intestine & bladder tone (motility) & ↓ sphincter tone
Eye	↑ contraction of sphincter (miosis) & ciliary muscle (NEAR vision)
Glands	↑ sweating, saliva, gastric acid secretion

Parasympathetic Agonist = Activation = INactivate sympathetic actions
(Think OPPOSITE of ALL sympathetic activation)

Parasympathetic Antagonist Effects

Heart	↑ CO = ↑ AV node firing = ↑ HR = TACHYcardia
Vascular musc.	NO EFFECT b/c NO innervation
Smooth musc.	Relaxation = ↓ GI & Urinary tract contraction
Eye	Pupil dilation & Loss of NEAR focus (FAR vision)
Glands	↓ sweat, saliva, gastric acid secretion
Central NS (CNS)	Belladonna Symptoms

Belladonna Symptoms: "mad as a hatter, red as a beet, blind as a bat, hot as hell, dry as a bone"

Eye Terminology

Miosis	Paralysis of ciliary muscle (loss of accommodation, ability to focus)
Mydriatic	Contraction of pupil (leads to pinpoint pupil, ie. Ach)
Cyclop-legia	Relaxation of pupil (dilation); Atropine: belladonna compound)

Antagonist: Parasympatholytic Agents

Antimuscarinic	Block ACh in Parasymp. Effector Junctions
Antinicotinic	Block ACh in Ganglia (Para- & Sympathetic; NN/N1)
Antinicotinic	Block ACh in NMJ (skeletal muscle relaxant, NM/N2)
Antinicotinic	Block ACh in Ganglia (both Para- & Sympathetic, NN/N1)



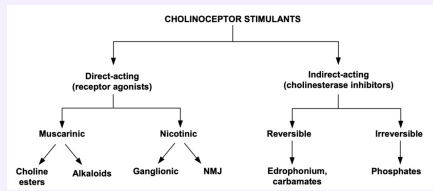
By Thomas Von Chao
(chautommy93)

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Agonist: Parasympathomimetic Agents



Directly-Acting: Combine with mACh and/or nAChs cholinceptors receptor directly → Direct activation.

Parasympathetic Agents

Agonist (1) Acetylcholine, ACh (2) Bethanecol (3) Pilocarpine (4) Methacholine

Antagonist (- tropine) (1) Atropine (2) Scopolamine (3) Homatropine (4) Benzotropine (5) pirenzepine

Directly-Acting PNS Agonist

mAChs	Choline Ester	Acetylcholine; Methacholine
		Carbachol; Bethanecol

	Alkaloids	Muscarine; Pilocarpine
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nAChs	Ganglionic Stimulants	Acetylcholine; Nicotine
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Varenicline (partial)

Choline Ester: Short-acting; stay in blood stream; NO (X) BBB

Alkaloids: (X) BBB

mAChs Agonists Uses

Acetylcholine	Ophthalmic (brief miosis)
Methacholine	Belladonna poisoning; Urinary retention
Bethanecol	Reverse post-op GI depression
Pilocarpine (alkaloid)	DOC for Glaucoma

Acetylcholinesterase Inhibitors (AChEIs)

Reversible	Edrophonium (Tensilon)	For myasthenia gravis (extreme muscle weakness)
Irreversible (comp. Inhibs)	Neostigmine	NO (X) BBB; For myasthenia gravis & ileus
	Physostigmine	(X) BBB; For glaucoma and for treatment of belladonna poisoning
	Pyridostigmine	Myasthenia gravis
	Amibenonium	Myasthenia gravis
Slow Reversible	Echothiophate	Glaucoma
	Organophosphate insecticides, nerve gases DFP	N/A
Inhibits AChE at both mAChs & nACh via ↑ synaptic concentration & half-life of Ach.		

Symptoms from Excess Cholinergic activity

General (SLUDE)	Salivation, Lacrimation, Urination, Diarrhea, Emesis
Muscarinic (SLUGBAM)	Salivation/Sz, Lacrimation, Urination, GI distress (D/V), Bronchoconstriction, Abd. cramps, Miosis
Nicotinic (MTWThF)	Mydriasis, Tachycardia, Weakness (muscle paralysis), hyperthermia, Fasciculation
Muscarinic (SLUGBAM)	Salivation/Sz, Lacrimation, Urination, GI distress (D/V), Bronchoconstriction, Abd. cramps, Miosis



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