Autonomic Nervous System

MOST FREQUENTLY USED DRUG CATEGORIES FOR AUTONOMIC SYSTEM THERAPY

Beta 1 Adrenergic Blockers (Anatgonists) - Work on the Heart

Beta 1 Adrenergic receptors are typically found on the heart and is a means for the sympathetic (adrenergic) nervous system to control heart rate. Therefore, Beta 1 Adrenergic Blockers block these receptors and limit heart rate. From an autonomic perspective, there are two classes of these drugs: peripherally acting (*e.g.*, Metaprolol, Toprol, Atenolol, and Propanolol), and centrally acting (*e.g.*, Acebutolol and Coreg). (Actually, Acebutolol and Coreg are known as cocktails, they contain more than one agent, and only one of their agents actually crosses into the brain.) The centrally acting Beta-Blockers, have a component that works in the brain stem and one or more components that work on the connection between the sympathetic nerves and the heart.

Beta 2 Adrenergic Agonists - Work in the Lungs

Beta 2 Adrenergic receptors are typically found on the smooth muscles that control the diameter of the bronchi in the lungs. Beta 2 Adrenergic Agonists stimulate these receptors to relax, opening airways and allowing more oxygen into the lungs. These drugs are typically used by asthmatics and other pulmonary patients as inhalants to treat the symptoms of spasmodic or constricted airways.

Alpha Adrenergic Agonists

Alpha Adrenergic receptors are typically found on the smooth muscles that control the diameter of the vasculature. Alpha Adrenergic Agonists (*e.g.*, Midodrine, a.k.a. ProAmatine) stimulate these receptors to constrict the vasculature and reduce the diameter and forcing blood to return to the heart.

Anti-Cholinergics (Cholinergic Anatgonists)

The cholinergic system is another name for the parasympathetic nervous system which is comprised mostly of the Vagus Nerve. Anti-Cholinergics (*e.g.*, Clonadine, and the side-effects of Tricyclic Anti-Depressants like Elavil or Amatriptyline and Nortriptyline) are drugs that limit the activity of the parasympathetic nervous system. These drugs help to treat disorders like depression, gastrointestinal upset, and fibromyalgia.

Angiotensin Blockers (Anatgonists)

The angiotensin-renin system is a part of the sympathetic nervous system that works with the kidneys to help control blood pressure. Angiotensin Blockers (*e.g.*, Angiotensin Converting Enzyme Inhibitors (ACE-Is) like Captopril, Benazepril, and Lisinopril; and Angiotensin II Receptor Blockers (ARBs) like Avapro or Irbesartan, Cozaar or Losartan and Diovan or Valsartan).

Calcium Channel Blockers (Anatgonists)

Calcium Channel are gated tunnels in the walls of cells that help to initiate the electrical activity in the cell that allows it to function. In the case of the cardiac muscles cells of the heart, it causes contraction. Calcium Channel Blockers (*e.g.*, Almodipine or Norvasc, Diltiazem or Cardizem, Vascor, and Verapamil) limit the ability of the "gate" to open, thereby limiting the ability of the cell to function. In this case, they limit the contraction of the cardiac muscles, which limits the force of contraction of the heart, thereby limiting or reducing blood pressure.

Antioxidants*

During chronic hyperglycemia, the metabolism of glucose also results in the generation of free radicals. Although free radicals of superoxide and hydrogen peroxide are essential for normal cell function, excessive accumulation of free radicals is detrimental and has a direct neurotoxic effect. a-Lipoic acid, an antioxidant that reduces free radical formation, appears to slow progression of CAN. For persons with type 2 diabetes, the improvement in CAN was seen after 4 months of treatment with an oral dosage of 800 mg/d (34). For persons with type 1 diabetes, the effect on autonomic function was seen after 10 d of 600 mg daily iv a-lipoic acid followed by 600 mg given orally for 50 d.

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Autonomic Nervous System

Sympathetic Nervous System

Promotes a "fight or flight" response, corresponds with arousal and energy generation, inhibits digestion:

- Diverts blood flow away from the gastro-intestinal (GI) tract and skin via vasoconstriction.
- Blood flow to skeletal muscles, the lung is not only maintained, but enhanced (by as much as 1200%, in the case of skeletal muscles).
- Dilates bronchioles of the lung, which allows for greater alveolar oxygen exchange.
- Increases heart rate and the contractility of cardiac cells (myocytes), thereby providing a mechanism for the enhanced blood flow to skeletal muscles.
- Dilates pupils and relaxes the lens, allowing more light to enter the eye.

Parasympathetic Nervous System

Promotes a "rest and digest" response; promotes calming of the nerves return to regular function, and enhances digestion.

- Dilates blood vessels leading to the GI tract, increasing blood flow. This is important following the consumption of food, due to the greater metabolic demands placed on the body by the gut.
- The parasympathetic nervous system can also constrict the bronchiolar diameter when the need for oxygen has diminished.
- During accommodation, the parasympathetic nervous system causes constriction of the pupil and lens.
- The parasympathetic nervous system stimulates salivary gland secretion, and accelerates peristalsis, so, in keeping with the rest and digest functions, appropriate PNS activity mediates digestion of food and indirectly, the absorption of nutrients.
- Is also involved in erection of genitals, via the pelvic splanchnic nerves 2–4.

Neurotransmitters and pharmacology

At the effector organs, sympathetic ganglionic neurons release noradrenaline (norepinephrine), along with other cotransmittors such as ATP, to act on adrenergic receptors, with the exception of the sweat glands and the adrenal medulla:

- Acetylcholine is the preganglionic neurotransmitter for both divisions of the ANS, as well as the postganglionic neurotransmitter of parasympathetic neurons. Nerves that release acetylcholine are said to be cholinergic. In the parasympathetic system, ganglionic neurons use acetylcholine as a neurotransmitter, to stimulate muscarinic receptors.
- At the adrenal cortex, there is no postsynaptic neuron. Instead the presynaptic neuron releases acetylcholine to act on nicotinic receptors.
- Stimulation of the adrenal medulla releases adrenaline (epinephrine) into the bloodstream which will act on adrenoceptors, producing a widespread increase in sympathetic activity.

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The following table reviews the actions of these neurotransmitters as a function of their receptors:

Heart		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
cardiac output	increases	M2: decreases
SA node: heart rate (chronotropic)	β1, β2: increases	M2: decreases
Atrial cardiac muscle: contractility (inotropic)	β1, β2: increases	M2: decreases
Ventricular cardiac muscle	β1, β2: increases contractility (inotropic), increases cardiac muscle automatically	M2: decreases (atria only)
conduction at AV node	β1: increasesβ1: increases conduction increases cardiac muscle automaticity	M2: decreases conduction Atrioventricular block

Blood Vessels		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
vascular smooth muscle	M3: contracts; α: contracts; β2: relaxes	---
Renal Artery	α1[3]: constricts	---
Larger coronary arteries	α1 and α2[4]: constricts [2]	---
Smaller coronary arteries	β2:dilates [5]	---
arteries to viscera	α: constricts	---
arteries to skin	α: constricts	---
arteties to brain	α1[6]: constricts [2]	---
arteries to erectil tissue	α1[7]: constricts	M3: dilates
arteries to salivary gland	α: constricts	M3: dilates
hepatic artery	β2: dilates	---
arteries to skeletal muscle	β2: dilates	---
Veins	α1 and α2 [8]: constricts, β2: dilates	

Other		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
platelets	α2: aggregates	---
mast cells - histamine	β2: inhibits	---

Respiratory System		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
smooth muscles of bronchioles	β2: relaxes (major contribution); α1: contracts (minor contribution)	M3: contracts

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Nervous System		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
pupil of eye	α1: relaxes	M3: contracts
ciliary muscle	β2: relaxes	M3: contracts

Digestive System		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
salivary glands: secretions	β: stimulates viscous, amylase secretions; α1 = stimulates potassium cation	M3: stimulates watery secretions
lacrimal glands (tears)	β2: Protein secretion	M3: increases
kidney (renin)	β2: secretes	---
parietal cells	---	M1: gastric acid secretion
liver	α1, β2: glycogenolysis, gluconeogenesis	---
adipose cells	β3: stimulates lipolysis	---
GI tract (smooth muscle) motility	α1, α2[10], β2: decreases	M1, M3: increases
sphincters of GI tract	α2 [2], β2: contracts	M3: relaxes
glands of GI tract	no effect	M3: secretes

Endocrine System		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
pancreas (islets)	α2: decreases secretion from beta cells, increases secretion from alpha cells	increases stimulation from alpha cells and beta cells
adrenal medulla	N: secretes epinephrine	---

Urinary system		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
bladder wall	β2: relaxes	contracts
ureter	α1: contracts	
sphincter	α1: contracts; β2 relaxes	Relaxes

Reproductive System		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
uterus	α1: contracts; β2: relaxes	---
genitalia	α: contracts	M3: erection

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Integument		
Target	Sympathetic (adrenergic, with exceptions)	Parasympathetic (muscarinic)
sweat gland secretions	M: stimulates (major contribution); α1: stimulates (minor contribution)	---
arrector pili	α1: stimulates	---