Autonomic Nervous System

Drugs

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Key Points
- Autonomic drugs work at the synapses,
- Drugs either suppress or magnify the sympathetic or parasympathetic effect,
- Drugs don’t work on a single target organ so there are side effects,
- Sympathetic effects are opposite of parasympathetic effects

Autonomic Nervous System

- The ANS functions as an automatic modulating system for many body functions
  - Regulation of blood pressure (BP), heart rate, gastrointestinal (GI) tract motility, salivary gland secretions, and bronchial smooth muscle
- The ANS relies on specific neurotransmitters and a variety of receptors to initiate functional responses in target tissues

Autonomic effects

Sympathetic
- Increase heart rate
- Increase BP
- Constrict vessels (blood, urinary)
- Dilate bronchioles (increase respiration)
- Increase mucous saliva (dry mouth)
- Decrease peristalsis
- Dilate pupils (mydriasis)

Parasympathetic
- Decrease heart rate
- Decrease BP
- Dilate vessels
- Decrease respiration
- Increase serous saliva
- Increase peristalsis
- Constrict pupils (myopia)

Functional Organization

- Almost all body tissues are innervated by the ANS
  - Many, but not all, organs receive both parasympathetic and sympathetic innervation
  - The response will be equal to the sum of excitatory and inhibitory influences of the two divisions of the ANS (if a tissue receives both innervations)
  - Sensory fiber in one division can influence motor fibers in the other

Drugs can modify ANS activity by:

- Synthesis
- Storage
- Release
- Receptor interaction
- Disposition
Neurotransmitters

- The specificity of the neurotransmitters and receptors dictates the tissue response
- Between preganglionic and postganglionic nerves: Acetylcholine is the neurotransmitter in the synapse. Nerves that release acetylcholine are termed cholinergic.
- Between postganglionic nerves and the effector tissues:
  - PANS: neurotransmitter released from the postganglionic nerve terminal is acetylcholine; aka cholinergic
  - SANS: Neuroepinephrine NE is the transmitter released by the postganglionic nerves and is designated as adrenergic

Basic Concept of Naming

- Drug that acts at location where acetylcholine is released as the neurotransmitter is termed cholinergic (from acetylcholine)
- Drug that acts at location where norepinephrine is neurotransmitter released is termed adrenergic (from early name of epinephrine, Adrenalin)
- Drug that acts at location where PANS acts has the prefix parasympatho-
- Drug that acts at location where the SANS acts has the prefix sympatho-
- Drug that acts at location where a division of the ANS acts and produces the same effect as the neurotransmitter has the suffix –mimetic (as in mime, acts like). Can also be referred to as agonist
- Drug that acts at the location where a division of the ANS acts and blocks the action of the neurotransmitter has the suffix lytic or –blocker. Can also be called an antagonist

4 Divisions of ANS Drugs

- P+:
  - Cholinergics
  - Parasympathomimetics
- P-:
  - Anticholinergics
  - Parasympatholytics
  - Cholinergic-blockers
- S+:
  - Sympathomimetics
  - Adrenergics
- S-:
  - Adrenergic-blockers
  - Sympathetic-blockers
  - Sympatholytics

Fate of Neurotransmitter

1. Diffuse out of the area (Norepinephrine and acetylcholine)
2. Enzymes (–ase) destroys it (acetylcholinesterase)
3. Reabsorbed (reuptake) to be used again (Norepinephrine)

Transmission across a synapse

- Neurotransmitter Chemical produced by body
- Receptors are different And have been identified alpha, beta 1, beta 2, gamma, etc
- Synaptic cleft
- Neurotransmitter receptors

Cholinergic (Parasympathomimetic) Agents

- Cholinergic agents are classified as direct acting (acts on receptor) or indirect acting (causes release of neurotransmitter)
  - Direct-acting agents include choline derivatives and pilocarpine
  - Indirect-acting parasympathomimetic agents or cholinesterase inhibitors act by inhibiting the enzyme cholinesterase
Pharmacologic Effects (Cholinergic)

- Cardiovascular effects
  - Direct effect on the heart produces a negative chronotropic and inotropic action
  - A decrease in cardiac output is associated with these agents
  - The effect on smooth muscle results in relaxation and vasodilation, producing a decrease in total peripheral resistance
  - The indirect effect is an increase in heart rate and cardiac output
  - Because direct and indirect effects are opposite, the effect will depend on the concentration of the drug present
  - Generally causes bradycardia and a decrease in BP and cardiac output

- GI effects
  - Cholinergic agents excite smooth muscle of the GI tract
  - Produces an increase in activity, motility, and secretion

Adverse Reactions (Cholinergic)

- Adverse reactions are extensions of the pharmacologic effects
- Large doses produce toxic effects described by the acronym SLUD (salivation, lacrimation, urination, and defecation)
- With even larger doses, neuromuscular paralysis can occur
- Treatment of an overdose of cholinesterase inhibitors such as insecticides or organophosphates (parathion) includes a combination of pralidoxime and atropine

Contraindications (Cholinergic)

- Relative contraindications or cautions
  - Bronchial asthma: cholinergic agents may cause bronchospasms or precipitate an asthmatic attack
  - Hyperthyroidism: may cause an increased risk of atrial fibrillation
  - GI or urinary tract obstruction: an increase in secretions and motility could cause pressure
  - Severe cardiac disease: reflex tachycardia may exacerbate a severe cardiac condition
  - Peptic ulcer: anticholinergic agents stimulate gastric acid secretion and increase gastric motility

Sympathetic Receptors

- Alpha – results in smooth muscle excitation or contraction; blood vessels (constriction), eye (mydriasis)
- Beta 1 – heart (increase rate and force)
- Beta 2 – bronchioles (dilation)

Sympathetic (SANS) Drugs

- SANS drugs work at synapse,
- Drugs have far reaching effect because synapse is in chain with other synapses,
- If drug increases effect, it’s called an “adrenergic” (adrenalin) agonist or “sympathomimetic”
- If drug decreases effect, it’s called “blocker” or adrenergic antagonist

Sympathomimetics

Mimics the neurotransmitter norepinephrine

Uses
- Vasoconstriction (epinephrine)
- BP elevator (epinephrine)
- Bronchodilator (pseudoephedrine, albuterol)
- Stimulator (amphetamine, Ritalin)
**Epinephrine**
- Anaphylaxis - increase BP, dilate bronchioles
- Anesthetic vasoconstrictor

**Phenylpropanolamine**
(mimics effects of epinephrine and norepinephrine)

**Pseudoephedrine**
(dilate bronchioles)

**Bronchodilator**
- Beta 2 agonist
  Causes bronchioles to dilate

**Sympathomimetic Concerns**
- Increases BP, hypertension concern
- Increases glycogenesis, diabetic concern
- Increases mucous saliva, dry mouth concern
- Increases nervousness, lower pain threshold

**Sympathetic Antagonists (blocker)**
- Beta blocker (Propranolol) - for arrhythmia, hypertension, angina
  - Can cross blood brain barrier and cause CNS suppression, xerostomia
  - Can precipitate asthma by constricting bronchioles
  - Orthostatic hypotension a possibility
Sympathetic Antagonists (blocker)

- Alpha blocker (Minipress, Hytrin, Cardura)
- Dilates blood vessels to decrease BP
- Other similar drugs used to treat Raynaud’s disease

Parasympathetic (PANS) Drugs

- Drugs work at synapse,
- Agonist drugs are called cholinergic (for acetylcholine) or parasympathomimetic,
- Antagonists are anticholinergic or cholinergic antagonists,

Direct vs Indirect effects

- Direct acting stimulate neurotransmitter production
- Indirect inhibit acetylcholinesterase so more acetylcholine available

Cholinergic Agonists

- Glaucoma – increased pressure in the eye, pupil dilates
- Cholinergic agent constricts pupil, decreases pressure
- Drug affects muscarinic sites, stimulates neurotransmitter production
- Pilocarpine, Carbachol common drugs
- Pilocarpine also used to treat xerostomia

Cholinergic Agonists

- myasthenia gravis – neuromuscular disorder with a gradual weakening of muscles, can’t hold eyes open, difficulty swallowing
- Anticholinesterase, nicotine receptor cholinergic agonists used to treat

Anticholinergics

- Atropine
  - Used before surgery to prevent aspiration
  - Used to treat GI spasms
  - Used in dentistry to temporarily cause xerostomia
  - Reduces the secretion of many organs
- Scopolamine used for motion sickness, CNS sedation
Anticholinergic Overdose

- Overdose causes adrenergic effects including tachycardia, dry mouth, restlessness, excitement, constipation