**Neurotransmitter Receptors**

**Neurotransmitters and Receptors**

- **Neurotransmitters** are chemicals that allow neurons (nerve cells) to communicate with each other, usually by being “released” into the small space between two neighbouring cells called a **synaptic cleft**.

- These neurotransmitters then freely bind to **receptors** on the postsynaptic cell, triggering a response (usually causing or inhibiting an action potential – see *Nerve Signal Transmission* handout) in that cell. Thus the neurotransmitters are considered **ligands** for their receptors.

- These receptors are **specific** to particular neurotransmitters, just like a lock and key.
  - For example, acetylcholine receptors can only interact with acetylcholine and not with dopamine or epinephrine.

- A neurotransmitter can bind to **multiple types of receptors** just like a master key in a building. This depends on the final desired physiological result; binding to some receptors can stimulate the recipient neuron to become active, but others can inhibit an already active neuron.

- **Agonists** (aka ligands) will activate a receptor and cause a response. In the lock and key scenario, the agonist would be the key. **Antagonists** will block a receptor from being activated by agonists. In the lock and key scenario, the key would break inside the lock, and no other keys could be used to open the lock.
Below are examples of two neurotransmitters and their different receptors that are particularly important for pharmacology. The effect of an agonist binding is described, and the main locations for these receptors are indicated in **bold**. Knowing the effects of each receptor agonist will help you figure out side effects of any drug. An antagonist binding to the receptors would have the opposite effect of what is written below (e.g. if an agonist causes constriction, an antagonist/blocker would cause dilation).

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<tr>
<th>Neurotransmitter</th>
<th>Receptor</th>
<th>Subtype</th>
<th>Function of Agonist</th>
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| Acetylcholine (ACh) | Muscarinic | **M₁** | - Parasympathetic organs other than the heart  
- Stimulates *gastric glands* to secrete acid, increases secretion of saliva  
- Stimulates smooth muscle  
- Involved in complex CNS responses |
| | | **M₂** | - Slows **heart** rate to normal  
- Decreases force of contraction in atria (but not ventricles) |
| | **M₃** | - Increases intracellular calcium causing constriction of smooth muscles including bronchoconstriction, constriction of the pupil, and increase motility of the gastrointestinal (GI) tract  
- Increases synthesis of nitric oxide in vascular cells causing vasodilation (*contradicts above point!*  
- Stimulates secretion from *exocrine and endocrine glands* (e.g. stomach secretions, saliva)  
- Regulates insulin secretion from pancreas |
| | | **M₄** | - Autoregulating - ACh decreases the release of ACh within the CNS (negative feedback) |
| | | **M₅** | - Found in both CNS and PNS, but function within the body is unclear |
| Nicotinic | **N₁ – N₄** | - Overall description of subtypes:  
- Stimulates skeletal muscle contraction at *neuromuscular junction* and postganglionic neurons by increasing Na⁺ and K⁺ permeability  
- Present on all *autonomic ganglia* and allow ACh to stimulate the post-ganglionic fibers of the PNS and SNS  
- Stimulates cells within the adrenal gland (i.e. medulla) |
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| Norepinephrine or Epinephrine | Adrenergic | α₁ | • All sympathetic target organs *except* the heart  
  • Causes *smooth muscle* contraction, including vasoconstriction in skin, mucosal membranes, and abdominal viscera; closure of sphincters along gastrointestinal (GI) tract and urinary bladder; dilation of pupils; bronchoconstriction  
  • Gluconeogenesis and glycogenolysis |
| | | α₂ | • Increases parasympathetic activity  
  • Inhibits release of norepinephrine from *presynaptic adrenergic nerve terminals*  
  • Cardiac muscle relaxation  
  • Platelet activation  
  • Decreases contraction/motility of GI walls |
| | | β₁ | • Increases *heart* rate and force of contraction  
  • Increases release of renin from *kidneys*  
  • Accelerates metabolic activities of *skeletal muscles*  
  • Increases lipolysis from fat tissues |
| | | β₂ | • Causes relaxation of *smooth muscle*, including vasodilation in skeletal and cardiac muscle, bronchodilation, decrease in GI tract motility, urinary retention  
  • Causes breakdown of glycogen in the *liver*  
  • Causes dilation in *blood vessels* to skeletal muscles, heart, and liver  
  • Inhibits histamine release from mast cells  
  • Increases renin secretion from kidneys |
| | | β₃ | • Causes breakdown of fat stores in *adipose tissue*  
  • Stimulates thermogenesis in *skeletal muscle*  
  • Promotes relaxation of bladder (prevents urination) |
Questions:

1. A patient has been prescribed a $\beta_2$-agonist for her asthma, but she is concerned about the side effects of this drug. Is this the correct drug for her diagnosis? What side effects could she encounter?

2. A patient comes in with tachycardia. The doctor prescribes two different drug types to ensure the tachycardia subsides. What two types of drugs would be logical? Why?

3. A patient who struggles to urinate has been prescribed an $\alpha_1$-antagonist. Is this the best choice of drug for the patient?

4. A new diet drug has come on the market that claims to have fewer side effects than the previous drug from the same receptor family. Which receptor would the new drug likely target? The old drug?

Answers:

1. A $\beta_2$-agonist would be the best drug in this situation because it causes bronchodilation. Some side effects she could encounter include problems urinating, constipation, potential for diabetes (high glucose concentration from glycogenolysis), and low blood pressure due to dilation of vessels.

2. A $\beta_1$-antagonist would help decrease the heart rate and force of contraction. Also, an $M_2$-agonist would slow the heart rate to normal. By combining these drugs, the physician can ensure a lowered heart rate by decreasing the sympathetic nervous system (the $\beta_1$-blocker) and by stimulating the parasympathetic nervous system (the $M_2$-agonist).

3. Normally, the $\alpha_1$ receptor causes constriction of the sphincter, which would decrease the ability to urinate. Therefore, giving an antagonist would relax the sphincters and help the patient urinate. A $\beta_2$-antagonist would also help because the bladder muscle (detrusor muscle) could contract easier.

4. The new drug would likely be a $\beta_3$-agonist because it would increase lipolysis with few side effects. The old drug could have been a $\beta_1$-agonist, which also triggers lipolysis, but side effects would include increases in heart rate and blood pressure (dangerous).