Week 1-Neurophysiology & Pharmacology

Many blood pressure medications work at the neurological level to treat hypertension (high blood pressure). Here is a list of the 5 classes of antihypertensive drugs (we will cover the kidney in the 2nd half of the semester, so don't focus on Diuretics or Angiotensin Disrupters):

1) Diuretics-help to reduce blood pressure by increasing excretion of ions in the kidneys (nephron, specifically), thus increasing water excretion via osmosis and decreasing blood volume.
   - Thiazides (e.g. Hydrochlorothiazide)-inhibit Na+ reabsorption in the distal convoluted tubule by competing with Na+/Cl- cotransporters.
   - Loop diuretics (e.g. Furosemide)-inhibit Na+ and Cl- reabsorption in the thick ascending Loop of Henle by blocking Na+/K+/2Cl- symporters.
   - Aldosterone blockers (e.g. Spironolactone)-inhibit Na+ reabsorption in the distal convoluted tubule and collecting duct by blocking the receptors of Aldosterone, the hormone responsible for the upregulation and activation of various Na+ channels and pumps in the nephron.

2) Anti-Adrenergics-help to reduce blood pressure by limiting the actions of epinephrine and norepinephrine, thereby reducing vasoconstriction and the contractility and force of the heart.
   - Peripheral blockers-prevent sympathetic stimulation of cardiac contractility and vasoconstriction by blocking neurotransmitters that activate those cells.
     - Alpha blockers (e.g. Doxazosin)-block alpha receptors in the heart and blood vessels, preventing neurotransmitter (mostly norepinephrine due to a decreased sensitivity to epinephrine) from causing overall vasoconstriction (more alpha receptors in the periphery).
     - Beta blockers (e.g. Propranolol)-block beta receptors in the heart and blood vessels, preventing neurotransmitter (mostly epinephrine for B2 due to decreased sensitivity to norepinephrine; B1 shows equal preference for

epinephrine and norepinephrine) from causing overall cardiac contraction (more beta receptors in the heart).

- Central blockers (e.g. Clonidine)-prevent sympathetic stimulation of blood pressure by blocking the neurotransmitters that activate those postganglionic nerves.

3) Direct-Acting Vasodilators (e.g. Hydralazine)-induces smooth muscle relaxation by binding and activating gated K+ channels, thus hyperpolarizing the membrane and preventing threshold from being reached.

4) Calcium-Channel Blockers (e.g. Amlodipine)-decrease cardiac contractility and induce vasodilation by blocking smooth muscle calcium channels, slowing the rate of calcium influx and muscle contraction.

5) Angiotensin Disrupters-decrease blood pressure by inhibiting the actions of Angiotensin II, which stimulates vascular smooth muscle contraction, Na+ reabsorption in the proximal tubules of the nephron, and secretion of Aldosterone.
   - ACE Inhibitors (e.g. Lisinopril)-prevent the conversion of Angiotensin I to Angiotensin II by inhibiting the enzyme responsible, Angiotensin-Converting Enzyme (ACE).
   - Angiotensin-Receptor Blockers (e.g. Losartan)-as the name states, these drugs block the receptors that recognize Angiotensin II.

It is important to note that neuropharmacology has wider applications than hypertension treatment, such as pain management (e.g. Lidocaine blocking Na+ channels and preventing pain signals from reaching the brain), anxiety (e.g. Diazepam allosterically increasing ligand binding of GABA to its receptors, which are Cl-specific channels, thus hyperpolarizing the membrane and reducing action potential firing), and psychiatric disorders (Serotonin and Dopamine potentiators that are beyond the scope of this class).