Autonomic Nervous System is a division of the nervous system separate from the somatic system which maintains body homeostasis by integrating signals from afferent somatic and visceral sensors to modulate organ perfusion and function. These signals are integrated in medulla and modulated by the central autonomic network which consists (in addition to the medulla) of the cerebral cortex, hypothalamus and amygdala. Information is then sent from the medulla to the effector organs by the different components of the ANS which are the parasympathetic and sympathetic nervous systems. Their tonic activity maintains cardiac activity and visceral and vascular smooth muscles in a state of immediate function from which rapid increases or decreases in autonomic outflow can adjust blood flow and organ activity in response to the environment.

Neurotransmitters of the ANS Acetylcholine is the principle transmitter released by preganglionic fibres of both the sympathetic and parasympathetic nervous systems (shown in blue on the adjacent diagram). The parasympathetic postganglionic fibres secrete acetylcholine onto their target organs, while noradrenaline is principally secreted by the postganglionic sympathetic fibres (red). The two exceptions to this are the adrenal medulla which acts as a postganglionic fibre itself and secretes 80% adrenaline and 20% noradrenaline into the systemic circulation, and sweat glands whose sympathetic postganglionic fibres secrete ACh. See also Al on neurotransmitters, and iontophores.

Receptors of the ANS Nicotinic receptors are ligand gated ion channels which are located in skeletal muscle, on postganglionic neurons in both the SNS and PNS, on adrenal chromaffin cells and within the CNS. Muscarinic receptors are seven transmembrane domain proteins coupled to a family of G Proteins that inhibit adenylyl cyclase activity. They are located on the heart where they are inhibitory, and in the smooth muscle and the glands where they are excitatory. Like the muscarinic receptors, adrenergic receptors are also seven transmembrane domain proteins coupled to G Proteins however there are multiple subtypes and actions. There are four major subtypes α₁α₂β₁ and β₂. Adrenoceptors respond to catecholamines in an order of potency; for alpha receptors this is noradrenaline ≥ adrenaline ≥ isoproterenol, for beta receptors it is adrenaline ≥ isoproterenol ≥ norad.

Sympathetic nervous system pharmacology (see neuropharmacology 2 for pharmacology related to the parasympathetic division of the ANS) The alpha adreceptors exist at both presynaptic and postsynaptic neuroeffector junction sites throughout the human body and are involved in cardiovascular regulation, metabolism, consciousness and nociception. Whilst there are at least six subtypes it is the alpha 1&2 subtypes which are the most important physiologically. It is possible to classify the differences in the two primary alpha receptors as shown below.

### Alpha 1 Adreceptors
- **Stimulated by:** Phenylephrine, Methoxamine
- **Blocked by:** Prazosin
- **Order of Potency:** noradrenaline ≥ isoproterenol
  - norad has greater potency vs α₁
- **G Protein Subtypes:** activates Gₛ and stimulates phospholipase C hydrolysis and increases intracellular Ca²⁺ levels
- **Physiological Effects:** Vasoconstriction, relaxation of GIT smooth muscle, contraction of genitourinary smooth muscles

### Alpha 2 Adreceptors
- **Stimulated by:** Clonidine, Dexametomidine
- **Blocked by:** Yohimbine
- **Order of Potency:** norad ≥ adrenaline ≥ isoproterenol
  - norad has lesser potency vs α₂
- **G Protein Subtypes:** activates Gₛ and results in decreased adenyl cyclase activation of cAMP
- **Physiological Effects:** Inhibition of noradrenaline release from nerve endings, platelet aggregation, vascular smooth muscle contraction

The beta adrenoceptors b Receptors regulate numerous functional responses, including heart rate and contractility, smooth muscle relaxation, and multiple metabolic events. All three of the b receptor subtypes (b₁, b₂, and b₃) couple to Gs and activate adenylyl cyclase. Thus, stimulation of b adrenergic receptors leads to the accumulation of cyclic AMP, activation of PKA, and altered function of numerous cellular proteins as a result of their phosphorylation. In addition, Gs can enhance directly the activation of voltage-sensitive Ca²⁺ channels in the plasma membrane of skeletal and cardiac muscle.

### Beta 1 Adreceptors
- **Stimulated by:** No selective agonist
- **Blocked by:** Esmolol, Metoprolol, Bisoprolol
- **Order of Potency:** isoproterenol ≥ adrenaline ≥ norad
- **G Protein Subtypes:** activates Gₛ increases cAMP through adenylyl cyclase activation
- **Physiological Effects:** Located at the SA and AV nodes and ventricular tissue, it increases inotropy and chronotropy

### Beta 2 Adreceptors
- **Stimulated by:** No selective antagonist but several non selective inc propanolol
- **Blocked by:** Salbutamol
- **Order of Potency:** isoproterenol ≥ adrenaline ≥ norad
- **G Protein Subtypes:** activates Gₛ increases cAMP through adenylyl cyclase activation
- **Physiological Effects:** Widespread distribution, located in bronchial and vascular smooth muscle, where they mediate vasodilation and bronchial relaxation