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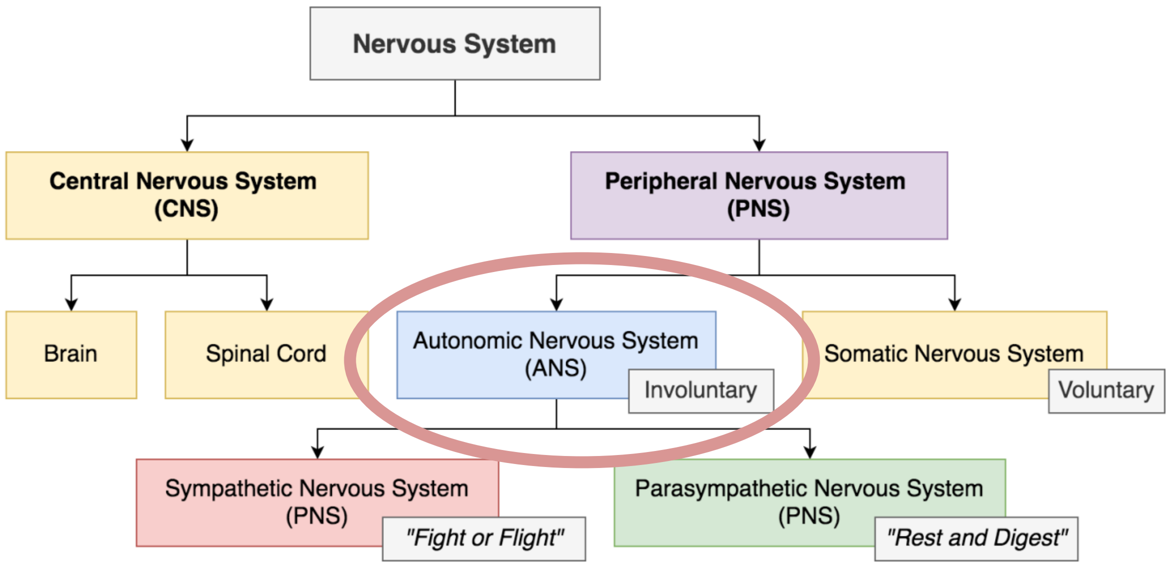
An introduction to the autonomic nervous system

By the perioperativeCPD team

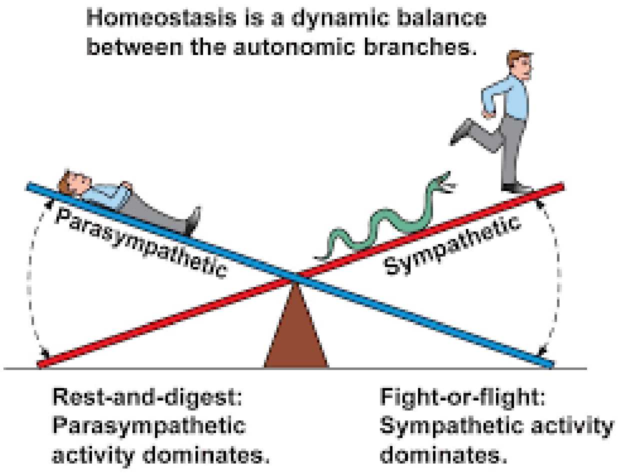
As many procedures and drugs used in anaesthetic practice have a direct influence on the autonomic nervous system, it is essential that the anaesthetic assistant should have an understanding of its structure and function although this is a very simplified introduction of a large and complex topic.

The autonomic nervous system is responsible for regulating many body processes including blood pressure, heart rate, digestion and even sweating. The system works automatically (autonomously), without a person's conscious effort and is part of the peripheral nervous system. The peripheral nervous system has several branches but this module will concentrate primarily on the autonomic nervous system with its sympathetic and parasympathetic divisions.



How does it affect the patient?

Anaesthetists constantly record and monitor patients' vital signs, markers of their autonomic nervous system activity, in order to maintain intraoperative homeostasis. They react to or even preempt any changes in homeostasis.



For example, a patient undergoing general anaesthesia for eye surgery is intubated with direct laryngoscopy. Direct laryngoscopy and tracheal intubation in patients with normal airway reflexes results in stimulation of the sympathetic nervous system. This, in turn, may lead to haemodynamic changes such as increased heart rate and elevated blood pressure. However if an opioid such as fentanyl is used prior to laryngoscopy it has the effect of blunting the response of the sympathetic system (as well as giving analgesia) therefore maintaining homeostasis.

Conversely, traction on the eyeball during surgery can activate the parasympathetic division via the ocular-cardiac reflex causing significant bradycardia. Atropine or glycopyrrolate can be given to block this parasympathetic response, increasing the heart rate and restoring homeostasis.

What is fight or flight?

The sympathetic side of the autonomic nervous system is often associated with the "fight-or-flight" response, which refers to the preparation of the body to either run away from a threat or to stand and fight in the face of that threat. To suggest what this means, consider the (very unlikely) situation of seeing a lioness hunting out on the African plains. Though this is not a common threat that humans deal with in the modern world, it represents the type of environment in which the human species thrived and adapted.

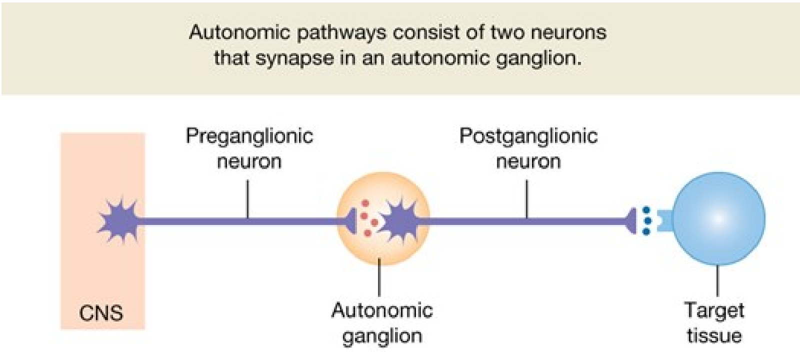
The reactions modern humans have in the modern world are based on these prehistoric situations. If your boss is walking down the corridor Friday afternoon looking for "volunteers" to cover the weekend on-call, your response is the same as the prehistoric human seeing the lioness hunting them across the savannah: fight or flight? Most likely, your response to your boss—not to mention the lioness—would be flight. Run away! The sympathetic side is responsible for the physiological response to make that possible, and hopefully successful. This is balanced by the parasympathetic side "rest and digest" both which are explained in more detail below.

Anatomy of the autonomic nervous system

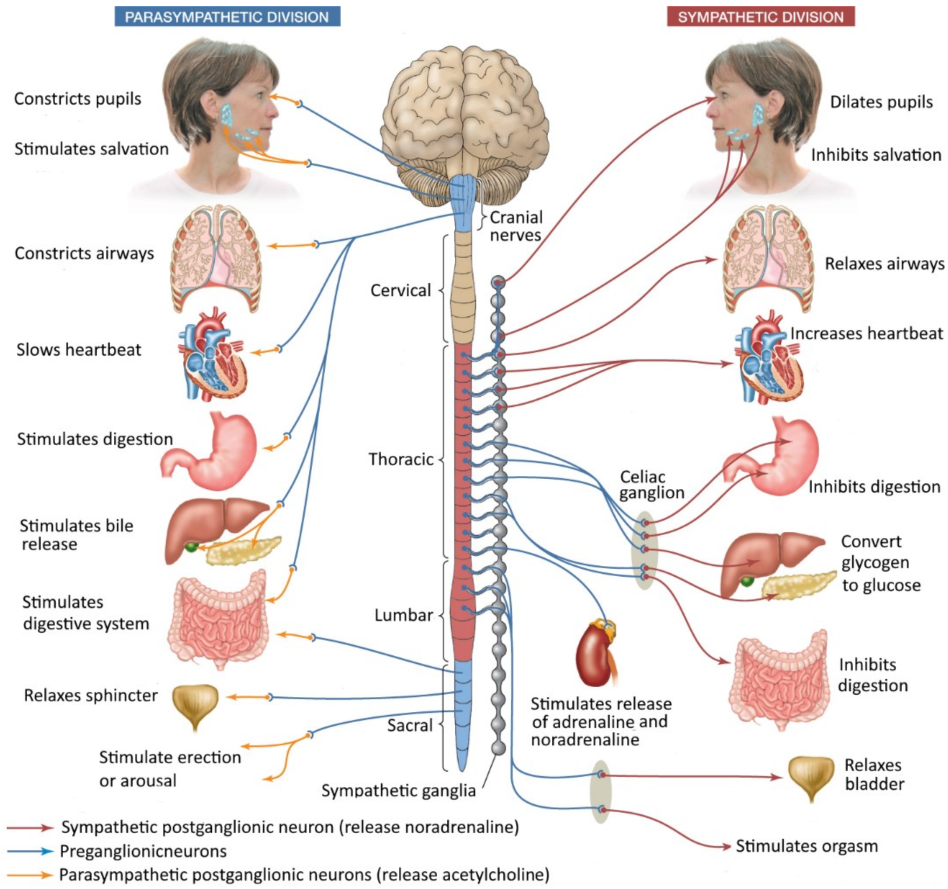
The autonomic nervous system is the part of the nervous system that innervates many of the bodies systems and organs and has two main divisions:

- Sympathetic division (fight or flight)
- Parasympathetic division (rest and digest)

Each of the autonomic nervous systems pathways involves two nerve cells. One cell is located in the brain stem or spinal cord. It is connected by nerve fibres to the other cell, which is located in a cluster of nerve cells called a ganglion. Nerve fibres from these ganglia connect with the target organs.



Most of the ganglia for the sympathetic division are located just outside the spinal cord on both sides of it (sympathetic ganglion). The ganglia for the parasympathetic division are located near or in the organs they connect with.



As the diagram above shows many organs are controlled by both the sympathetic and the parasympathetic divisions and have opposite effects on the same organ. For example, the sympathetic division increases heart rate, and the parasympathetic division decreases it. Overall, the two divisions work together to ensure that the body responds appropriately to different situations and homeostasis is maintained. Note that control of most of the parasympathetic nervous system is via the vagus nerve and over stimulation of the vagus nerve is the cause of vasovagal syncope.

Sympathetic division of the autonomic nervous system

Generally, the **sympathetic division** prepares the body for stressful or emergency situations—fight or flight

Examples of the effect of the sympathetic nervous system are as follows.

Heart	Increases the heart rate Increases the strength of cardiac contraction
Blood vessels	Vasoconstriction (in non-essential vascular smooth muscle) Vasodilatation (in vital cardiac vessels and lungs)
Lungs	Bronchodilatation
Energy Metabolism	Increases glycogenolysis in the liver Increases glucagon release from the pancreas Reduces insulin release from the pancreas In general makes glucose and fat available for energy
Eyes	Dilates pupil Focuses the eye for distance vision
GI Tract	Decreases peristalsis Contracts sphincters
Bladder	Constricts sphincter
Skin	Increases sweating Contracts erector pili muscles (makes hairs stand on end to help cooling)

Many of the above functions are cooperative. The heart is stimulated to increase cardiac output. Airflow into the lungs is improved to meet an increased demand for oxygen. Glucose and fatty acids are mobilised from their respective reserve stores in the liver and adipose tissue so that they are available for the skeletal muscles, heart and brain. The GI tract and bladder are put into a dormant state in order to reduce their energy and blood flow requirements. Dilatation of the pupil allows more light to enter the eye which improves sensitivity to movement (although at the expense of a loss of fine detail) and the lens shifts to distance vision to detect incoming attacks and the skin sweats to prevent overheating. This gives us the best chance of ‘flight’.

Adrenergic receptors (sympathetic nervous system)

Although the autonomic nervous system communicates through nerve fibres, the junctions between these fibres (synapses) and between the nerve fibres and the target organs rely on chemical messengers known as neurotransmitters. The main neurotransmitters involved in stimulating organs in the sympathetic nervous system are adrenaline and noradrenaline*. Fibres that secrete adrenaline and noradrenaline are called adrenergic fibres.

* American terms for adrenaline and noradrenaline are epinephrine and norepinephrine

Generally noradrenaline is released at the nerve ending of the target organ; while adrenaline is mostly released by the body into the bloodstream from the adrenal gland and causes widespread sympathetic stimulation. Both bind onto and activate adrenergic receptors located on the target organs.

Alpha and beta receptors are the main sympathetic or adrenergic receptors involved in the sympathetic nervous systems fight-or-flight mechanism.

- alpha-1 and alpha-2 (α1, α2)
- beta-1 and beta-2 (β1, β2)

Others such as the beta-3 (β3) are responsible for long term processes such as breaking down fat for energy but are not covered here.

Alpha-1

Alpha-1 receptors are located primarily on smooth muscle including arteries and veins. When the alpha-1 receptors are stimulated (by noradrenaline released at the sympathetic nerve ending or adrenaline released into the bloodstream) it results in the constricting of both peripheral arteries and veins; however, the vasoconstrictor effect is more pronounced in the arteries as they contain more smooth muscle. This constriction of the small arteries and arterioles increases systemic vascular resistance, therefore the blood pressure (BP=CO x SVR) and causes a diversion of blood flow from the peripheries to the vital organs.

These alpha-1 receptors can also be stimulated by **metaraminol** and **phenylephrine**, which are specific alpha-1 agonists stimulating only the alpha-1 receptors, therefore causing peripheral vasoconstriction which consequently increases the blood pressure.

Remember an agonist is a chemical that binds to a receptor and activates it to produce a biological response. In contrast, an antagonist blocks the action of the given receptor.

Alpha-2

Alpha-2 receptors are a little different as alpha-2 stimulation inhibits noradrenaline release thus inhibiting sympathetic activity and therefore lowering the blood pressure and heart rate but they are minor players compared with alpha-1 receptors.

The two major drugs relevant to anaesthetics in this group are **clonidine** and **dexmedetomidine** which are used for treating hypertension and for its sedating effects. If both alpha-1 and alpha-2 receptors are stimulated then the alpha-1 effects dominate.

Beta-1

Beta-1 receptors are located mainly in the heart. When beta-1 receptors are stimulated they increase cardiac output, by raising the heart rate (positive chronotropic effect), and increasing contraction (positive inotropic effect). This helps move more oxygen to the vital organs and muscles ready to 'fight or flight'.

Dobutamine and **Isoprenaline** are cardiac stimulants which act on beta-1 receptors and increase contractility. **Dobutamine** is used to increase cardiac output in someone experiencing acute heart failure or shock.

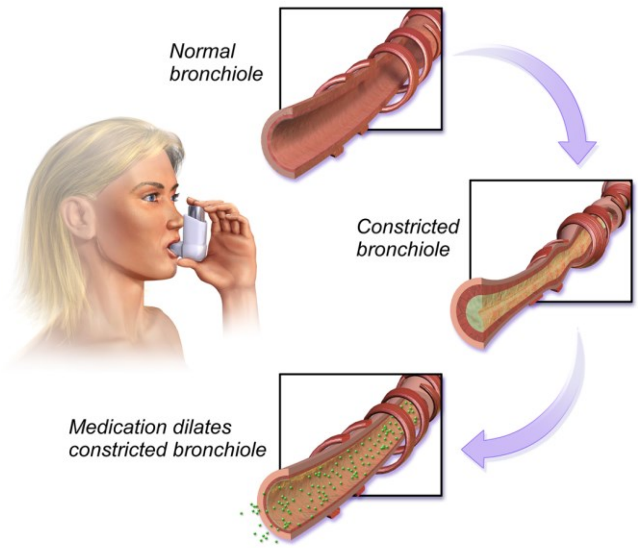
We can also use a beta-1 antagonist (beta-blocker) such as **metoprolol** which inhibit beta-1 receptors thus decreasing heart rate and contractility which in turn decreases blood pressure for the hypertensive patient and reduces the chance of a dysrhythmia after a heart attack.

Sometimes we want to increase the heart rate, cardiac output and blood pressure, then we can use **ephedrine** which stimulates both alpha and beta receptors for 10-15 minutes.

Beta-2

Beta-2 receptors are located mainly in the lungs and the arteries of the cardiac and skeletal muscles. When these receptors are stimulated they increase the diameter of the bronchioles to let more air in and out during breathing. The arteries in cardiac and skeletal muscle also vasodilate as both of these require increased blood flow to assist the flight or flight response.

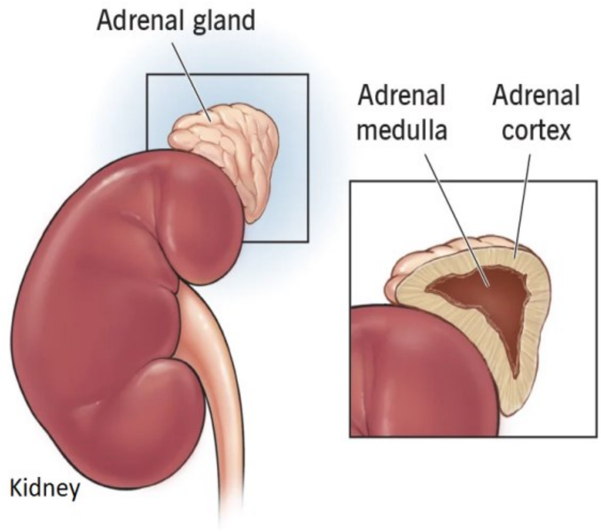
Salbutamol is an example of a beta-2 agonist or bronchodilator; which is used to relieve symptoms of asthma and chronic obstructive pulmonary disease.



Stimulating Beta 2 Receptors in the Lungs

Adrenal Medulla and Adrenaline

The adrenal gland which sits on top of each kidney is a bonus feature of the sympathetic nervous system. No equivalent structure exists for the parasympathetic nervous system. The adrenal medulla (the inner part of the adrenal gland) synthesises noradrenaline (20%) and adrenaline (80%), which are collectively known as catecholamines. Both adrenaline and noradrenaline can stimulate the adrenoreceptors used by sympathetic nerve fibres to communicate with their target cells.



The adrenal gland releases adrenaline and noradrenaline into the blood and therefore provides a systemic boost to the whole sympathetic nervous system across multiple organs.

Therefore when we administer adrenaline to a patient we expect short acting alpha-1, alpha-2, beta-1 and beta-2 agonist effects which gives a:

- Increase in blood pressure
- Increased heart rate
- Increased cardiac contractility
- Dilation of the bronchioles in the lungs
- Dilation of the vessels in the skeletal muscles

Parasympathetic division of the autonomic nervous system

The **parasympathetic division** controls body process during ordinary situations- rest and digest.

Examples of actions of the parasympathetic nervous system are as follows.

Heart	Decreases heart rate
Blood vessels	No effect in most blood vessels
Lungs	Bronchoconstriction
Energy Metabolism	Deceases glucagon release from the pancreas Increases insulin secretion from the pancreas
Eyes	Constricts pupil, focuses the eye for near vision
GI Tract	Stimulates the secretion of large volumes of watery saliva Promotes the secretion of gastric acid Increases peristalsis, relaxes sphincters
Bladder	Relaxes sphincter

The range of actions of the parasympathetic nervous system is less than that of the sympathetic. The effects on the heart are limited to heart rate whereas the sympathetic nervous system affects both heart rate and the strength of heart (myocardial) contraction.

The parasympathetic nervous system has one of its strongest associations with the GI tract and the process of digestion; 'rest and digest'. The secretion of saliva is stimulated to facilitate chewing and initiate digestion. The production of gastric acid is increased, as are the secretions of the small and large bowel. Having primed the GI tract to receive the meal, the parasympathetic nervous system also invigorates the smooth muscle of the GI tract to undertake mechanical digestion and movement of the meal.

Cholinergic receptors (parasympathetic)

The parasympathetic system also has receptors, these are called cholinergic receptors. There are two types, muscarinic receptors and nicotinic receptors but the nicotinic receptors are only involved in muscle contraction, and can be blocked by muscle relaxants (neuromuscular blocking agents to be exact) such as suxamethonium and rocuronium. As a result we can mostly ignore them for this module. Although not entirely as there is some crossover, which is why when you give neostigmine to reverse the action of muscle relaxants, there is a parasympathetic response and sudden bradycardia results if glycopyrrolate or atropine are not co-administered.

This leaves one type of parasympathetic receptor, the muscarinic receptor (remember this is a very simplified view). When this receptor is stimulated by the release of acetylcholine, the main neurotransmitter for the parasympathetic nervous system, it causes a decrease in the heart rate and an increase in digestion, i.e rest and digest.

What would happen if we block the parasympathetic muscarinic receptors? That would cause the heart rate to increase, dilation of the bronchioles and less production of secretions in the body as the sympathetic side would take over. This is the exact effect of **atropine** and **glycopyrrolate**, drugs we use to counteract too much parasympathetic activity.

Note: in this very simplified description of a complicated topic, deeper reading can be found in any anatomy and physiology text book.

Summary

- The autonomic nervous system (ANS) is part of the peripheral nervous system and controls basic bodily functions that are regulated at an unconscious level.
- The sympathetic nervous division (SNS) prepares the body for 'fight or flight'.
- The parasympathetic nervous division (PNS) allows the body to 'rest and digest'.
- Adrenaline and noradrenaline simulate the sympathetic nervous system.
- When SNS alpha-1 receptors are stimulated it results in vasoconstriction and an increase in blood pressure (metaraminol, phenylephrine).
- SNS beta-1 stimulation results in increased heart rate and contractibility (Dobutamine and Isoprenaline specifically as well as ephedrine and adrenaline)
- SNS Beta-2 stimulation result in bronchiole dilatation (Salbutamol for asthmatics)
- Acetylcholine is the neurotransmitter for the parasympathetic nervous system and lowers the heart rate.
- If the parasympathetic (muscarinic) receptors are blocked (atropine/glycopyrrolate) it causes an increase in the heart rate and a drying of secretions.

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