

# Sympathetic nervous system

The **sympathetic nervous system** (**SNS**) is one of the three divisions of the <u>autonomic nervous system</u>, the others being the <u>parasympathetic nervous system</u> and the <u>enteric nervous system</u>. The enteric nervous system is sometimes considered part of the autonomic nervous system, and sometimes considered an independent system.

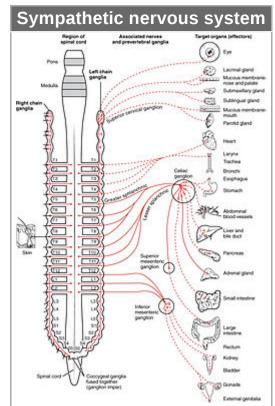
The autonomic nervous system functions to regulate the body's unconscious actions. The sympathetic nervous system's primary process is to stimulate the body's <u>fight or flight response</u>. It is, however, constantly active at a basic level to maintain <u>homeostasis</u>. The sympathetic nervous system is described as being antagonistic to the parasympathetic nervous system. The latter stimulates the body to "feed and breed" and to (then) "rest-and-digest".

The SNS has a major role in various physiological processes such as blood glucose levels, body temperature, cardiac output, and immune system function. The formation of sympathetic neurons being observed at embryonic stage of life and its development during aging shows its significance in health; its dysfunction has shown to be linked to various health disorders. [5]

# Structure

There are two kinds of <u>neurons</u> involved in the transmission of any signal through the sympathetic system: pre-ganglionic and post-ganglionic. The shorter <u>preganglionic neurons</u> originate in the <u>thoracolumbar division</u> of the <u>spinal cord</u> specifically at  $\underline{T1}$  to  $\underline{L2\sim L3}$ , and travel to a <u>ganglion</u>, often one of the <u>paravertebral ganglia</u>, where they synapse with a postganglionic neuron. From there, the long <u>postganglionic</u> neurons extend across most of the body. [6]

At the synapses within the ganglia, preganglionic neurons release acetylcholine, a neurotransmitter that activates nicotinic acetylcholine receptors on postganglionic neurons. In response to this stimulus, the postganglionic neurons release norepinephrine, which activates adrenergic receptors that are present on the peripheral target tissues. The activation of target



Schematic illustration showing the sympathetic nervous system with sympathetic cord and target organs.

sympathetic cord and target organs.			
Details			
Identifiers			
<u>Latin</u>	pars sympathica		
	divisionis autonomici		
	systematis nervosi		
Acronym(s)	SNS		
MeSH	D013564 (https://meshb.		
	nlm.nih.gov/record/ui?ui=		
	D013564)		
TA98	A14.3.01.001 (https://ifa		
	a.unifr.ch/Public/EntryPag		
	e/TA98%20Tree/Entity%2		
	0TA98%20EN/14.3.01.00		
	1%20Entity%20TA98%20		
	EN.htm)		
TA2	6601 (https://ta2viewer.o		
	penanatomy.org/?id=660		
	1)		

tissue receptors causes the effects associated with the sympathetic system. However, there are three important exceptions:  $\boxed{7}$ 

1. Postganglionic neurons of <u>sweat glands</u> release acetylcholine for the activation of <u>muscarinic</u> receptors, except for areas of thick skin, the palms and the plantar surfaces of the feet, where norepinephrine is released and acts on adrenergic receptors. This leads to the activation of <u>sudomotor</u>

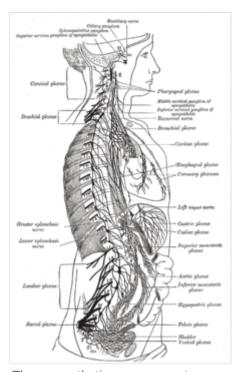
FMA	9906 (https://bioportal.bio
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	d=http%3A%2F%2Fpurl.
	org%2Fsig%2Font%2Ffm
	a%2Ffma9906)
Anatomical terminology	

- receptors. This leads to the activation of <u>sudomotor</u> function which is assessed by electrochemical skin conductance.
- 2. Chromaffin cells of the adrenal medulla are analogous to post-ganglionic neurons; the adrenal medulla develops in tandem with the sympathetic nervous system and acts as a modified sympathetic ganglion. Within this endocrine gland, pre-ganglionic neurons synapse with chromaffin cells, triggering the release of two transmitters: a small proportion of norepinephrine, and more substantially, epinephrine. The synthesis and release of epinephrine as opposed to norepinephrine is another distinguishing feature of chromaffin cells compared to postganglionic sympathetic neurons. [8]
- 3. Postganglionic sympathetic nerves terminating in the <u>kidney</u> release <u>dopamine</u>, which acts on <u>dopamine D1 receptors</u> of blood vessels to control how much blood the kidney filters. <u>Dopamine</u> is the immediate metabolic precursor to <u>norepinephrine</u>, but is nonetheless a distinct signaling molecule. [9]

#### Organization

Sympathetic nerves arise from near the middle of the spinal cord in the intermediolateral nucleus of the lateral grey column, beginning at the first thoracic vertebra of the vertebral column and are thought to extend to the second or third lumbar vertebra. Because its cells begin in the thoracolumbar division – the thoracic and lumbar regions of the spinal cord – the sympathetic nervous system is said to have a thoracolumbar outflow. Axons of these nerves leave the spinal cord through the anterior root. They pass near the spinal (sensory) ganglion, where they enter the anterior rami of the spinal nerves. However, unlike somatic innervation, they quickly separate out through white rami connectors (so called from the shiny white sheaths of myelin around each axon) that connect to either the paravertebral (which lie near the vertebral column) or prevertebral (which lie near the aortic bifurcation) ganglia extending alongside the spinal column.

To reach target organs and glands, the axons must travel long distances in the body, and, to accomplish this, many axons relay their message to a second cell through <u>synaptic transmission</u>. The ends of the axons link across a space, the <u>synapse</u>, to the <u>dendrites</u> of the second cell. The first cell (the presynaptic cell) sends a <u>neurotransmitter</u> across the synaptic cleft where it activates the second cell (the postsynaptic cell). The message is then carried to the final destination.



The sympathetic nervous system extends from the thoracic to lumbar vertebrae and has connections with the thoracic, abdominal, and pelvic plexuses.

Presynaptic nerves' axons terminate in either the <u>paravertebral</u> ganglia or <u>prevertebral</u> ganglia. There are four different paths an axon can take before reaching its terminal. In all cases, the axon enters the paravertebral ganglion at the level of its originating spinal nerve. After this, it can then either synapse in this ganglion, ascend to a more superior or descend to a more inferior paravertebral ganglion and synapse there, or it can descend to a prevertebral ganglion and synapse there with the postsynaptic cell. [10]

The postsynaptic cell then goes on to innervate the targeted end effector (i.e. gland, smooth muscle, etc.). Because paravertebral and prevertebral ganglia are close to the spinal cord, presynaptic neurons are much shorter than their postsynaptic counterparts, which must extend throughout the body to reach their destinations.

A notable exception to the routes mentioned above is the sympathetic innervation of the suprarenal (adrenal) medulla. In this

Spiral nerve

Spiral nerve

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Scheme showing structure of a typical <u>spinal nerve</u>. 1. Somatic efferent. 2. Somatic afferent. 3,4,5. Sympathetic efferent. 6,7. Sympathetic afferent.

case, presynaptic neurons pass through paravertebral ganglia, on through prevertebral ganglia and then synapse directly with suprarenal tissue. This tissue consists of cells that have pseudo-neuron like qualities in that when activated by the presynaptic neuron, they will release their neurotransmitter (epinephrine) directly into the bloodstream.

In the sympathetic nervous system and other components of the peripheral nervous system, these synapses are made at sites called ganglia. The cell that sends its fiber is called a preganglionic cell, while the cell whose fiber leaves the ganglion is called a <u>postganglionic</u> cell. As mentioned previously, the preganglionic cells of the sympathetic nervous system are located between the first thoracic segment and the third lumbar segments of the spinal cord. Postganglionic cells have their cell bodies in the ganglia and send their axons to target organs or glands.

The ganglia include not just the sympathetic trunks but also the <u>cervical ganglia</u> (superior, <u>middle</u> and <u>inferior</u>), which send sympathetic nerve fibers to the head and thorax organs, and the <u>celiac</u> and <u>mesenteric</u> ganglia, which send sympathetic fibers to the gut.

Autonomic nervous system's jurisdiction to organs in the human body

Organ	Nerves <sup>[11]</sup>	Spinal column origin <sup>[11]</sup>
stomach	<ul> <li>PS: anterior and posterior vagal trunks</li> <li>S: greater splanchnic nerves</li> </ul>	<u>T5, T6, T7, T8, T9,</u> sometimes
duodenum	<ul> <li>PS: <u>vagus nerves</u></li> <li>S: greater splanchnic nerves</li> </ul>	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$
jejunum and ileum	<ul><li>PS: posterior vagal trunks</li><li>S: greater splanchnic nerves</li></ul>	<u>T5, T6, T7, T8, T9</u>
spleen	S: greater splanchnic nerves	<u>T6, T7, T8</u>
gallbladder and liver	<ul> <li>PS: vagus nerve</li> <li>S: celiac plexus</li> <li>right phrenic nerve</li> </ul>	<u>T6, T7, T8, T9</u>
colon	<ul> <li>PS: vagus nerves and pelvic splanchnic nerves</li> <li>S: lesser and least splanchnic nerves</li> </ul>	<ul> <li>T10, T11, T12 (proximal colon)</li> <li>L1, L2, L3, (distal colon)</li> </ul>
pancreatic head	<ul><li>PS: vagus nerves</li><li>S: thoracic splanchnic nerves</li></ul>	<u>T8</u> , <u>T9</u>
appendix	<ul> <li>nerves to superior mesenteric plexus</li> </ul>	<u>T10</u>
bladder	<ul> <li>PS: pelvic splanchnic nerves to detrusor muscles</li> <li>S: inferior hypogastric nerves</li> </ul>	S2-S4
kidneys and ureters	<ul> <li>PS: vagus nerve</li> <li>S: thoracic and lumbar splanchnic nerves</li> </ul>	<u>T11</u> , <u>T12</u>

#### Information transmission

Messages travel through the sympathetic nervous system in a bi-directional flow. Efferent messages can trigger changes in different parts of the body simultaneously. For example, the sympathetic nervous system can accelerate heart rate; widen bronchial passages; decrease motility (movement) of the large intestine; constrict blood vessels; increase peristalsis in the oesophagus; cause pupillary dilation, piloerection (goose bumps) and perspiration (sweating); and raise blood pressure. One exception is with certain blood vessels such as those in the cerebral and coronary arteries, which dilate (rather than constrict) with an increase in sympathetic tone. This is because of a proportional increase in the presence of  $\beta_2$ 



Sympathetic nervous system – Information transmits through it affecting various organs.

adrenergic receptors rather than  $\alpha_1$  receptors.  $\beta_2$  receptors promote vessel dilation instead of constriction like  $\alpha_1$  receptors. An alternative explanation is that the primary (and direct) effect of sympathetic stimulation

on coronary arteries is vasoconstriction followed by a secondary vasodilation caused by the release of vasodilatory metabolites due to the sympathetically increased cardiac inotropy and heart rate. This secondary vasodilation caused by the primary vasoconstriction is termed functional sympatholysis, the overall effect of which on coronary arteries is dilation. [12] The target synapse of the postganglionic neuron is mediated by adrenergic receptors and is activated by either norepinephrine (noradrenaline) or epinephrine (adrenaline).

# **Function**

(but also all other sympathetic fibers)

The sympathetic nervous system is		
responsible for up- and down-regulating	0	Effect
many homeostatic mechanisms in living	Eye	Dilates pupil
organisms. Fibers from the SYNS	ricart	Increases rate and force of contraction
innervate tissues in almost every organ system, providing at least some	Lungs	Dilates bronchioles via circulating adrenaline <sup>[13]</sup>
regulation of functions as diverse as	Blood vessels	Dilate in skeletal muscle <sup>[14]</sup>
pupil diameter, gut motility, and urinary	Digootivo oyotoiii	Constricts in gastrointestinal organs
system output and function. [15] It is perhaps best known for mediating the	Sweat diangs	Activates <u>sudomotor</u> function and sweat secretion
neuronal and hormonal stress response	Digoctive treet	Inhibits peristalsis
commonly known as the fight-or-flight		Increases renin secretion
response. This response is also known	Penis	Causes erection
as <i>sympatho-adrenal response</i> of the	Ductus deferens	Promotes emission prior to ejaculation
body, as the <u>preganglionic</u> sympathetic fibers that end in the <u>adrenal medulla</u>		tic system action on various organs <sup>[8]</sup> except where otherwise indicated.

secrete acetylcholine, which activates the great secretion of adrenaline (epinephrine) and to a lesser extent noradrenaline (norepinephrine) from it. Therefore, this response that acts primarily on the cardiovascular system is mediated directly via impulses transmitted through the sympathetic nervous system and indirectly via catecholamines secreted from the adrenal medulla.

The sympathetic nervous system is responsible for priming the body for action, particularly in situations threatening survival. One example of this priming is in the moments before waking, in which sympathetic outflow spontaneously increases in preparation for action.

Sympathetic nervous system stimulation causes vasoconstriction of most blood vessels, including many of those in the skin, the digestive tract, and the kidneys. This occurs as a result of activation of alpha-1 adrenergic receptors by norepinephrine released by post-ganglionic sympathetic neurons. These receptors exist throughout the vasculature of the body but are inhibited and counterbalanced by beta-2 adrenergic receptors (stimulated by epinephrine release from the adrenal glands) in the skeletal muscles, the heart, the lungs, and the brain during a sympathoadrenal response. The net effect of this is a shunting of blood away from the organs not necessary to the immediate survival of the organism and an increase in blood flow to those organs involved in intense physical activity.

#### **Sensation**

The afferent fibers of the <u>autonomic nervous system</u>, which transmit sensory information from the internal organs of the body back to the central nervous system (or CNS), are not divided into parasympathetic and sympathetic fibers as the efferent fibers are. [17] Instead, autonomic sensory information is conducted by general visceral afferent fibers.

General visceral afferent sensations are mostly unconscious visceral motor reflex sensations from hollow organs and glands that are transmitted to the <u>CNS</u>. While the unconscious <u>reflex arcs</u> normally are undetectable, in certain instances they may send <u>pain</u> sensations to the CNS masked as <u>referred pain</u>. If the <u>peritoneal cavity</u> becomes inflamed or if the bowel is suddenly distended, the body will interpret the afferent pain stimulus as <u>somatic</u> in origin. This pain is usually non-localized. The pain is also usually referred to dermatomes that are at the same spinal nerve level as the visceral afferent synapse.

### Relationship with the parasympathetic nervous system

Together with the other component of the <u>autonomic nervous system</u>, the parasympathetic nervous system, the sympathetic nervous system aids in the control of most of the body's internal organs. Reaction to <u>stress</u>—as in the flight-or-fight response—is thought to be elicited by the sympathetic nervous system and to counteract the <u>parasympathetic system</u>, which works to promote maintenance of the body at rest. The comprehensive functions of both the parasympathetic and sympathetic nervous systems are not so straightforward, but this is a useful rule of thumb. [4][18]

# **Origins**

It was originally believed that the sympathetic nervous system arose with <u>jawed vertebrates</u>. However, the sea lamprey (Petromyzon marinus), a <u>jawless vertebrate</u>, has been found to contain the key building blocks and developmental controls of a sympathetic nervous system. Nature described this research as a "landmark study" that "point to a remarkable diversification of sympathetic neuron populations among vertebrate classes and species". [21]

# **Disorders**

The dysfunction of the sympathetic nervous system is linked to many health disorders, such as <u>heart failure</u>, gastrointestinal problems, <u>immune dysfunction</u> as well as, <u>metabolic disorders</u> like, <u>hypertension</u> and diabetes. Highlighting the importance of the sympathetic nervous system for health.

The sympathetic stimulation of metabolic tissues is required for the maintenance of metabolic regulation and feedback loops. The dysregulation of this system leads to an increased risk of neuropathy within metabolic tissues and therefore can worsen or precipitate <u>metabolic disorders</u>. An example of this includes the retraction of sympathetic neurons due to leptin resistance, which is linked to obesity. [22] Another example, although more research is required, is the observed link that diabetes results in the impairment of synaptic transmission due to the inhibition of <u>acetylcholine receptors</u> as a result of high blood glucose levels. The loss of sympathetic neurons is also associated with the reduction of insulin secretion and impaired glucose tolerance, further exacerbating the disorder. [23]

The sympathetic nervous system holds a major role in long-term regulation of hypertension, whereby the central nervous system stimulates sympathetic nerve activity in specific target organs or tissues via neurohumoral signals. In terms of hypertension, the overactivation of the sympathetic system results in

vasoconstriction and increased heart rate resulting in increased blood pressure. In turn, increasing the potential of the development of cardiovascular disease. [24]

In <u>heart failure</u>, the sympathetic nervous system increases its activity, leading to increased force of muscular contractions that in turn increases the <u>stroke volume</u>, as well as peripheral <u>vasoconstriction</u> to maintain <u>blood pressure</u>. However, these effects accelerate disease progression, eventually increasing mortality in heart failure. [25]

Sympathicotonia is a stimulated  $\frac{[26]}{}$  condition of the sympathetic nervous system, marked by  $\frac{\text{vascular}}{}$  spasm,  $\frac{[27]}{}$  elevated blood pressure,  $\frac{[27]}{}$  and goose bumps.  $\frac{[27]}{}$ 

Heightened sympathetic nervous system activity is also linked to various mental health disorders such as, anxiety disorders and <u>post-traumatic stress disorder</u> (PTSD). It is suggested that the overactivation of the SNS results in the increased severity of PTSD symptoms. In accordance with disorders like hypertension and cardiovascular disease mentioned above, PTSD is also linked with the increased risk of developing mentioned diseases, further correlating the link between these disorders and the SNS. [28]

The sympathetic nervous system is sensitive to stress, studies suggest that the chronic dysfunction of the sympathetic system results in migraines, due to the vascular changes associated with tension headaches. Individuals with migraine attacks are exhibited to have symptoms that are associated with sympathetic dysfunction, which include reduced levels of plasma norepinephrine levels, sensitivity of the peripheral adrenergic receptors. [29]

Insomnia is a sleeping disorder, that makes falling or staying asleep difficult, this disruption in sleep results in sleep deprivation and various symptoms, with the severity depending on whether the insomnia is acute or chronic. The most favoured hypothesis for the cause of insomnia is the hyperarousal hypothesis, which is known as a collective over-activation of various systems in the body, this over-activation includes the hyperactivity of the SNS. Whereby during sleep cycle disruption sympathetic baroreflex function and neural cardiovascular responses become impaired. [30][31]

However more research is still required, as methods used in measuring SNS biological measures are not so reliable due to the sensitivity of the SNS, many factors easily effect its activity, like stress, environment, timing of day, and disease. These factors can impact results significantly and for more accurate results extremely invasive methods are required, such as microneurography. The difficultly of measuring the SNS activity does not only apply to insomnia, but also with various disorders previously discussed. However, overtime with advancements in technology and techniques in research studies the disruption of the SNS and its impact on the human body will be explored further. [32][33]

# History and etymology

The name of this system can be traced to the concept of <u>sympathy</u>, in the sense of "connection between parts", first used medically by <u>Galen</u>. In the 18th century, <u>Jacob B. Winslow</u> applied the term specifically to nerves. [35]

The concept that an independent part of the nervous system coordinates body functions had its origin in the works of Galen (129–199), who proposed that nerves distributed spirits throughout the body. From animal dissections he concluded that there were extensive interconnections from the spinal cord to the viscera and from one organ to another. He proposed that this system fostered a concerted action or 'sympathy' of the

organs. Little changed until the Renaissance when Bartolomeo Eustacheo (1545) depicted the sympathetic nerves, the vagus and adrenal glands in anatomical drawings. Jacobus Winslow (1669–1760), a Danishborn professor working in Paris, popularised the term 'sympathetic nervous system' in 1732 to describe the chain of ganglia and nerves which were connected to the thoracic and lumbar spinal cord. [36]

# See also

- Cremaster muscle
- Cremasteric reflex
- Epinephrine
- History of catecholamine research
- Limbic system
- Norepinephrine
- Sympathetic ganglia
- Sympathetic trunk
- Sympathicolysis

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