

# HYPOTHALAMUS AND AUTONOMIC NERVOUS SYSTEM

## A. Hypothalamus = Homeostasis

The main function of the hypothalamus is **homeostasis**, or maintaining the body's status quo. Factors such as blood pressure, body temperature, fluid and electrolyte balance, and body weight are held to a precise value called the set-point. Although this set-point can migrate over time, from day to day it is remarkably fixed.

To achieve this task, the hypothalamus must receive inputs about the state of the body, and must be able to initiate compensatory changes if anything drifts out of whack. The inputs include:

- **nucleus of the solitary tract** - this nucleus collects all of the visceral sensory information from the vagus and relays it to the hypothalamus and other targets. Information includes blood pressure and gut distension.
- **reticular formation** - this catchall nucleus in the brainstem receives a variety of inputs from the spinal cord. Among them is information about skin temperature, which is relayed to the hypothalamus.
- **retina** - some fibers from the optic nerve go directly to a small nucleus within the hypothalamus called the **suprachiasmatic nucleus**. This nucleus regulates circadian rhythms, and couples the rhythms to the light/dark cycles.
- **circumventricular organs** - these nuclei are located along the ventricles, and are unique in the brain in that they lack a blood-brain barrier. This allows them to monitor substances in the blood that would normally be shielded from neural tissue. Examples are the **OVL**, which is sensitive to changes in osmolarity, and the **area postrema**, which is sensitive to toxins in the blood and can induce vomiting. Both of these project to the hypothalamus.
- **limbic and olfactory systems** - structures such as the amygdala, the hippocampus, and the olfactory cortex project to the hypothalamus, and probably help to regulate behaviors such as eating and reproduction.

The hypothalamus also has some intrinsic receptors, including **thermoreceptors** and **osmoreceptors** to monitor temperature and ionic balance, respectively.

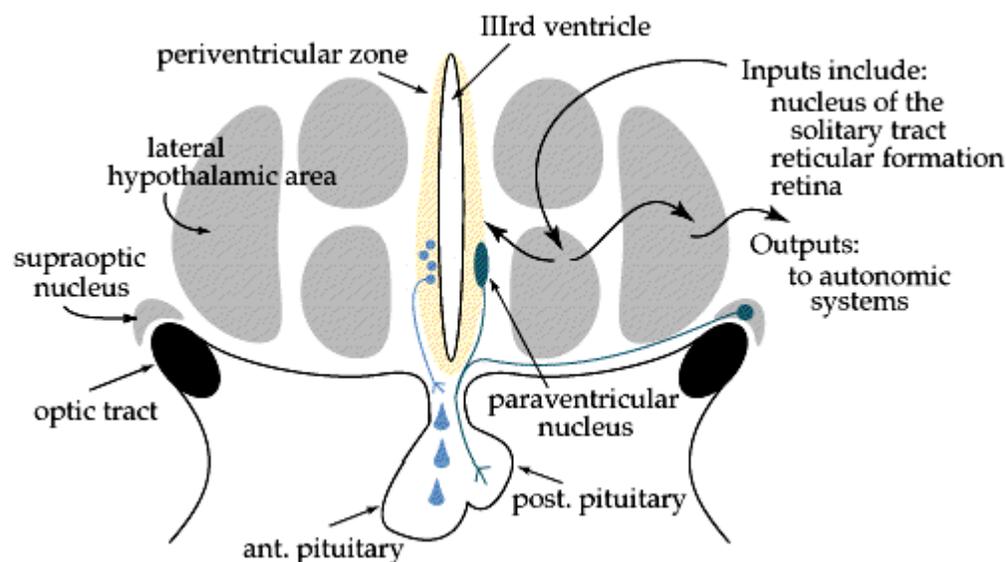
Once the hypothalamus is aware of a problem, how does it fix it? Essentially, there are two main outputs:

- **neural signals to the autonomic system** - the (lateral) hypothalamus projects to the (lateral) medulla, where the cells that drive the autonomic systems are located. These include the parasympathetic vagal nuclei and a group of cells that descend to the sympathetic system in the spinal cord. With access to these systems, the hypothalamus can

control heart rate, vasoconstriction, digestion, sweating, etc.

- **endocrine signals to/through the pituitary** - recall that an endocrine signal is a chemical signal sent via the bloodstream. Large hypothalamic cells around the third ventricle send their axons directly to the **posterior pituitary**, where the axon terminals release **oxytocin** and **vasopressin** into the bloodstream. Smaller cells in the same area send their axons only as far as the base of the pituitary, where they empty **releasing factors** into the capillary system of the **anterior pituitary**. These releasing factors induce the anterior pituitary to secrete any one of at least six hormones, including **ACTH** and **thyroid-stimulating hormone (TSH)**.

Ultimately the hypothalamus can control every endocrine gland in the body, and alter blood pressure (through vasopressin and vasoconstriction), body temperature, metabolism (through TSH), and adrenaline levels (through ACTH).



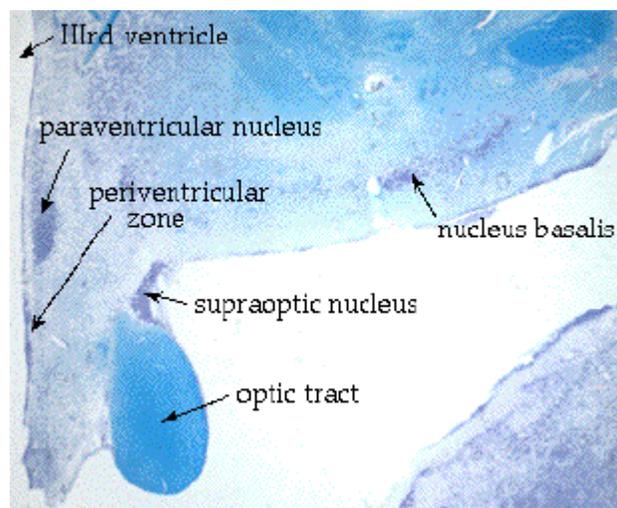
**In the news lately:** The hypothalamus controls body weight and appetite, but it is not entirely clear how. Sensory inputs, including taste, smell, and gut distension, all tell the hypothalamus if we are hungry, full, or smelling a steak. Yet it is mysterious how we are able to vary our eating habits day to day and yet maintain about the same weight (sometimes despite all efforts to the contrary!). The "set-point" theory is an old one in diet science, but until recently the mechanics of maintaining that set point were unknown. It appears that there is an endocrine component to the appetite system. Recent studies in mice have shown that the fat cells of normal overfed mice will release a protein called **leptin** (or **OB**, after the gene name), which reduces appetite and perks up metabolism. Leptin is presumably acting on the hypothalamus. Underfed mice, on the other hand, produce little or no leptin, and they experience an increase in appetite and a decrease in metabolism. In both of these mice, the result is a return to normal weight. But what would happen if a mouse (or human) had a defective OB gene? Weight gain would never trigger fat cells to release leptin, the hypothalamus would never slow the appetite or increase metabolism, and the mouse would

slowly but surely become obese (how the gene got its name). Sure enough, shortly after these experiments hit the news, the human OB gene was discovered and a few obese patients were found to have the mutation. Many more obese patients had normal OB genes, however, indicating that there is much more to the story yet to be discovered.

## B. The anatomy of the hypothalamus:

The hypothalamus, as you would expect from the name, is located below the thalamus on either side of the third ventricle. These sections have been cut coronally, and show only one side of the hypothalamus.

In this anterior section through hypothalamus, you can see the large neurons of the paraventricular nucleus, which send axons to the posterior pituitary. The cells in the periventricular zone send axons to the median eminence, from which releasing factors are carried to the anterior pituitary.

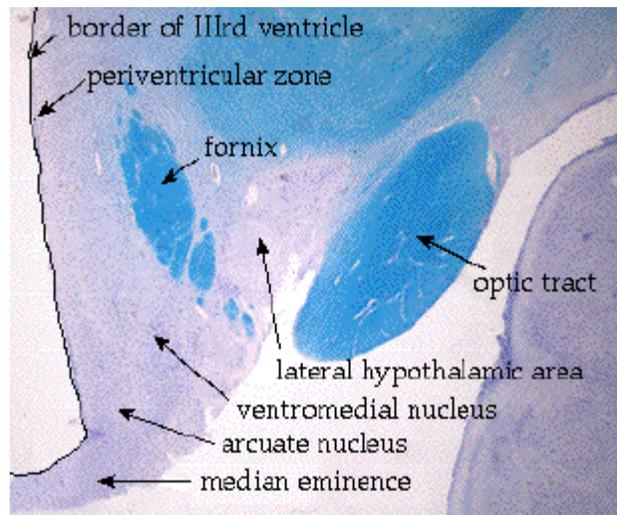


The nucleus basalis is a cholinergic nucleus involved in sleep and wakefulness.

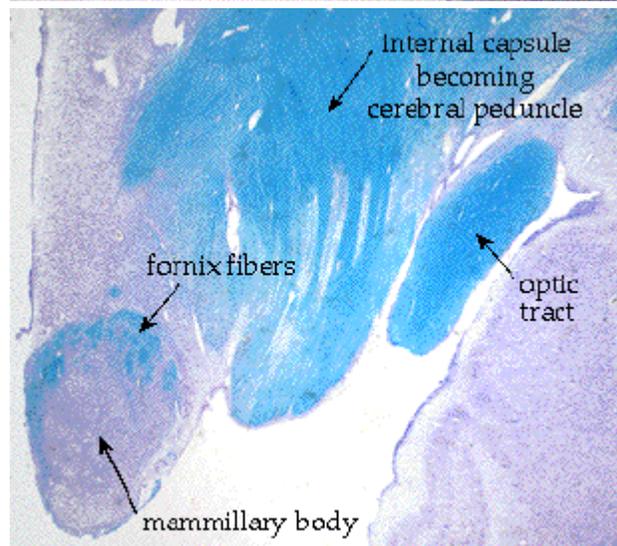
This section is posterior to the first. The hypothalamic nuclei are hard to distinguish, but the arrows point out approximate locations. The pituitary stalk would normally be continuous with the median eminence, but it is a fragile structure usually lost in dissection.

Note the fornix descending through the

hypothalamus. The fornix originates in the hippocampus and ends in the mammillary bodies.



In this posterior section you can see the fornix joining the mammillary body. This is also a nice section to demonstrate the way that the internal capsule fibers flow into the cerebral peduncle.



### C. The autonomic nervous system:

The autonomic nervous system is an entire little brain unto itself; its name comes from "autonomous", and it runs bodily functions without our awareness or control. It is divided into two systems which, where they act together, often oppose each other: the **sympathetic** and **parasympathetic** systems. The sympathetic system evokes responses characteristic of the "fight-or-flight" response: pupils dilate, muscle vasculature dilates, the heart rate increases, and the digestive system is put on hold. The parasympathetic system has many specific functions, including slowing the heart, constricting the pupils, stimulating the gut and salivary glands, and other responses that are not a priority when being "chased by a tiger". The state of the body at any given time represents a balance between these two systems.

The best way to learn the functions and structures of each system is by comparison. The following table lists some attributes of each:

<b>The Parasympathetic System</b>	<b>The Sympathetic System</b>
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Origins:

Parasympathetic cells are located in different nuclei throughout the **brainstem**, as well as a few in the **sacral spinal cord**. Their axons travel to the target organ, synapse in **ganglia** in or near the organ wall, and finally innervate the organ as "post-ganglionics".

Examples of these ganglia include the ciliary, otic, and pterygopalatine ganglia in the head, and diffuse networks of cells in the walls of the heart, gut, and bladder.

Nuclei of origin:

**Edinger- Westphal nucleus -**

Axons from this nucleus travel with cranial nerve III and have 2 functions:

- pupil constriction
- lens accommodation

**Salivatory nuclei** - These nuclei in the medulla send axons to the salivary glands via the VIIth and IXth nerves.

**Dorsal nucleus of the vagus -**

This nucleus gives rise to the secretomotor fibers of the vagus nerve (X). Its functions include:

- stimulate gastric secretion
- stimulate gut motility
- stimulate respiratory secretions

**Nucleus ambiguus** (and surrounding cells) - Axons from these cells project via the vagus to the heart, lungs, and pharynx.

Functions include:

- decrease heart rate
- bronchial constriction

The cells of the **intermediolateral column** in the **thoracic spinal cord** are the source of all the sympathetics. They also travel to ganglia before reaching the target organ, but the sympathetic ganglia are often far from the target. Some notable ganglia:

**Superior cervical ganglion -**

supplies sympathetics to the head, including those that:

- dilate the pupils
- stimulate sweat glands
- lift the eyelids

**Celiac and mesenteric ganglia -**

These ganglia distribute sympathetics to the gut. Functions include:

- vasoconstriction
- inhibition of secretions

**Chain ganglia** running along the spinal cord distribute sympathetics to the thorax and periphery to:

- increase heart rate
- dilate bronchi
- selectively vasoconstrict
- vasodilate in active muscles

The autonomic system also receives **afferents** that carry information about the internal organs. They return to separate locations:

#### Parasympathetic afferents

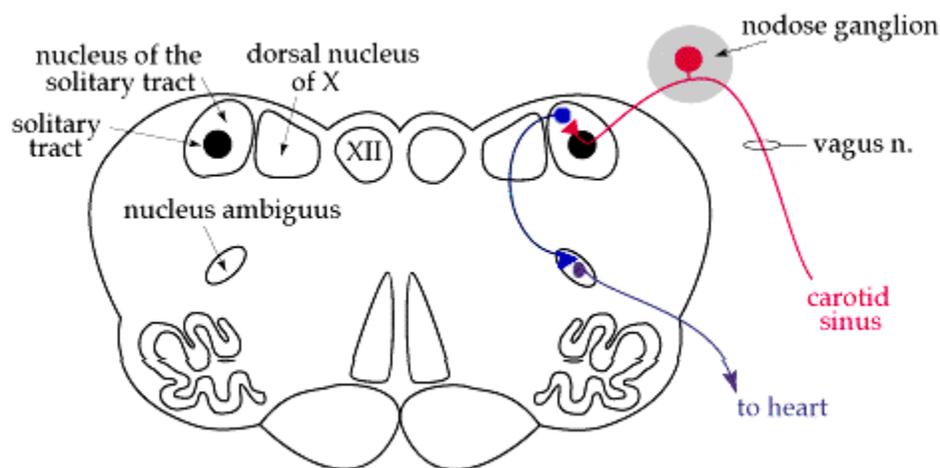
Nearly all of the afferents return via the vagus to a single nucleus, the **nucleus of the solitary tract**. Like all sensory afferents, the actual cell bodies of the neurons sit just outside the CNS in a ganglion (the **nodose ganglion**). The central processes of the neurons enter the medulla in the **solitary tract** and travel a bit before synapsing in the surrounding nucleus of the solitary tract. The solitary tract is somewhat analogous to Lissauer's tract in the spinal cord.

The nucleus receives information about blood pressure, carbon dioxide levels, gut distention, etc.

#### Sympathetic afferents

Afferents reenter the dorsal horn of the spinal cord along side of the sensory afferents from the skin. The sympathetic afferents mainly carry information about visceral pain. Since this information converges with pain from the body surface, the pain is often perceived as originating at the body surface instead of deep in the viscera. This phenomenon is called **referred pain**, and follows predictable patterns. For example, afferents from the heart enter the spinal cord at the same level as those from the shoulder region. This is why pain in the heart (a heart attack) is often referred to the shoulder.

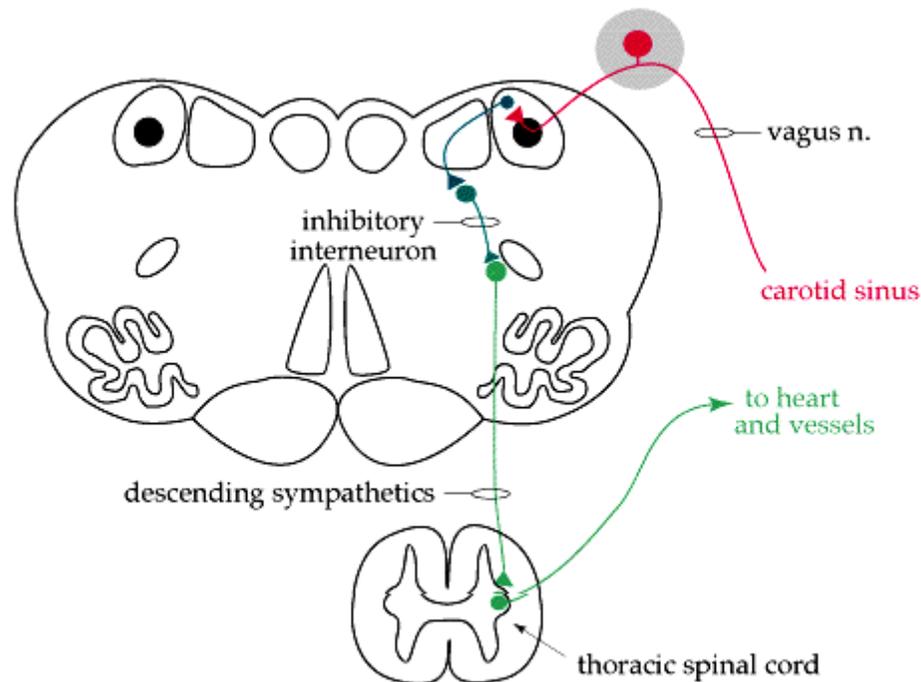
**D. The baroreceptor reflex:** A reflex is a pathway with an afferent signal (sensory) that evokes an efferent response (motor). The most common example is the stretch reflex, or knee-jerk reflex. A quick stretch of the tendon causes a brief contraction of the muscle. The autonomic system has several similar reflexes. One of these is the baroreceptor reflex, which maintains a constant blood pressure despite standing up or lying down.



The afferent signal comes from baroreceptors in the carotid sinus, a swelling of the carotid

artery in the neck. If blood pressure suddenly jumps up, the baroreceptors respond and send the signal back to the nucleus of the solitary tract (NTS). Neurons in the NTS project to an adjacent vagal nucleus, the nucleus ambiguus, and excite the neurons that project to the heart. These acetylcholinergic neurons slow the heart, bringing down the blood pressure a little.

However, there is more to the story. In the knee-jerk reflex, for the quadriceps muscle to contract briefly, the hamstring muscle must also relax briefly. As a flexor-extensor pair, they must always receive opposite signals. The sympathetic and parasympathetic systems are like a flexor-extensor pair, so when activating the parasympathetic you must inhibit the sympathetic. Just like in the spinal cord, this is accomplished by an inhibitory interneuron.



When the high blood pressure signal arrives at the NTS, an inhibitory interneuron projects to the group of cells that control the sympathetic neurons in thoracic cord. These cells are called the **descending sympathetics**. An important feature of the descending sympathetics is that they are constantly firing at a steady level. This enables them to be turned down - if a neuron was already silent, an inhibitory signal would make no difference. Therefore, in response to the surge in blood pressure, the descending sympathetics are inhibited, and the sympathetics in the spinal cord fire at a much lower rate. As a result, the heart and the blood vessels are allowed to relax, the heart slows, vasodilation occurs, and blood pressure drops. The inhibition of the sympathetic system is actually a more powerful way to lower blood pressure than activating the parasympathetic system.

[RETURN TO HOME PAGE](#)