Raja N. L. Khan Womens' College (Autonomous)

Zoology (H), 6th SEM, Paper DSE3T-Endocrinology

by M. Malik Mukherjee

Hypothalamus

Study Areas-

A) Structure
B) Functions (With reference to nuclei)
C) Regulation of Neuroendocrine glands
D) Feedback mechanisms

Hypothalamus is a very important part of the central nervous system present in the forebrain. It controls the firing of the autonomic nervous system as well as the functioning of the endocrine system. Thus, it plays a central role in controlling all the essential processes of life.

A) Structure:

I. Anatomical Features

In this section, we will discuss the location, structure, input and output fibres and blood supply of hypothalamus.

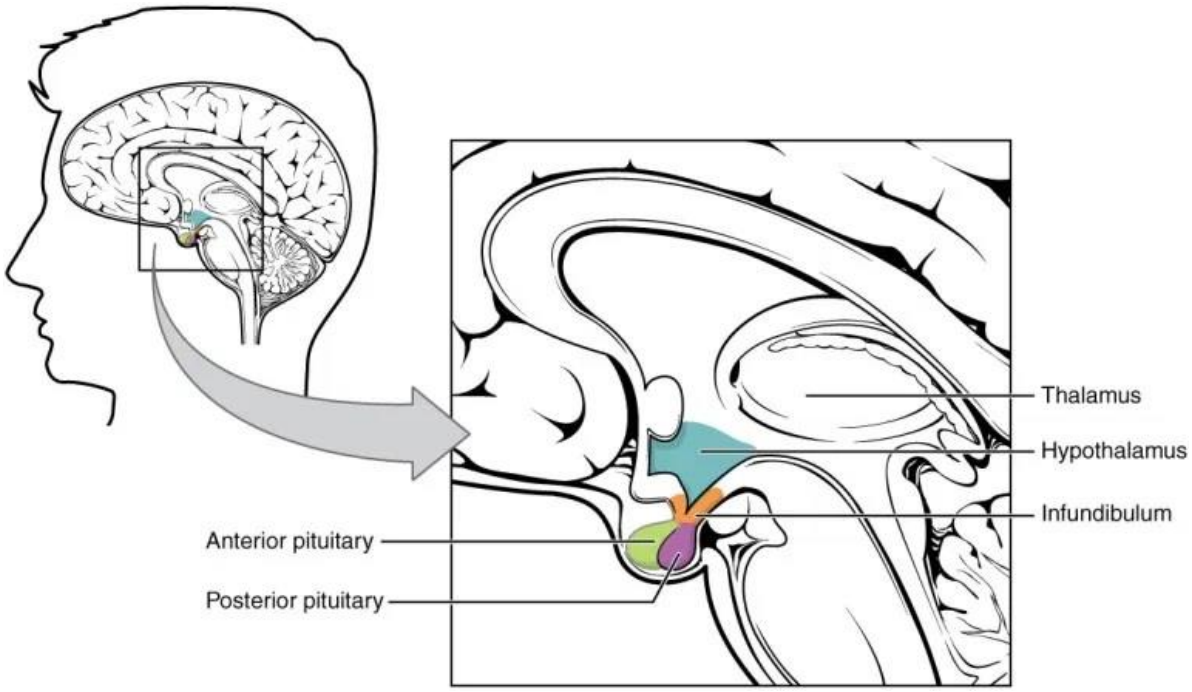
II. Location

According to the typical division of the brain into the forebrain, midbrain, and hindbrain, the hypothalamus is a **part of the forebrain**. It is considered to be a part of the diencephalon.

Hypothalamus is located just below the thalamus and forms the floor and the lower part of the lateral walls of the third ventricle. Anteriorly, it extends up to the optic chiasma and posteriorly it is continuous with the tegmentum of midbrain.

III. Structure

The **structure of the hypothalamus** is composed of a cluster of neurons that are arranged into nuclei. These nuclei send and receive fibres to other parts of the brain. For the purpose of understanding, the nuclei are divided into two groups; medial zone and lateral zone.



Lateral zone

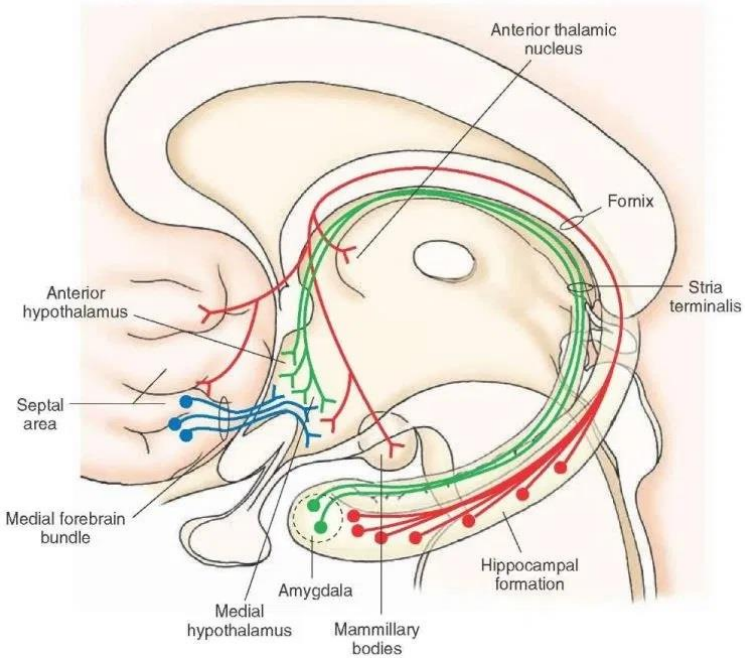
The lateral zone of the hypothalamus contains the following nuclei:

- Part of the preoptic nucleus
- Part of suprachiasmatic nucleus
- Lateral nucleus
- Tuberomammillary nucleus
- Lateral tubular nuclei

Medial zone

The medial zone of the hypothalamus contains the following nuclei:

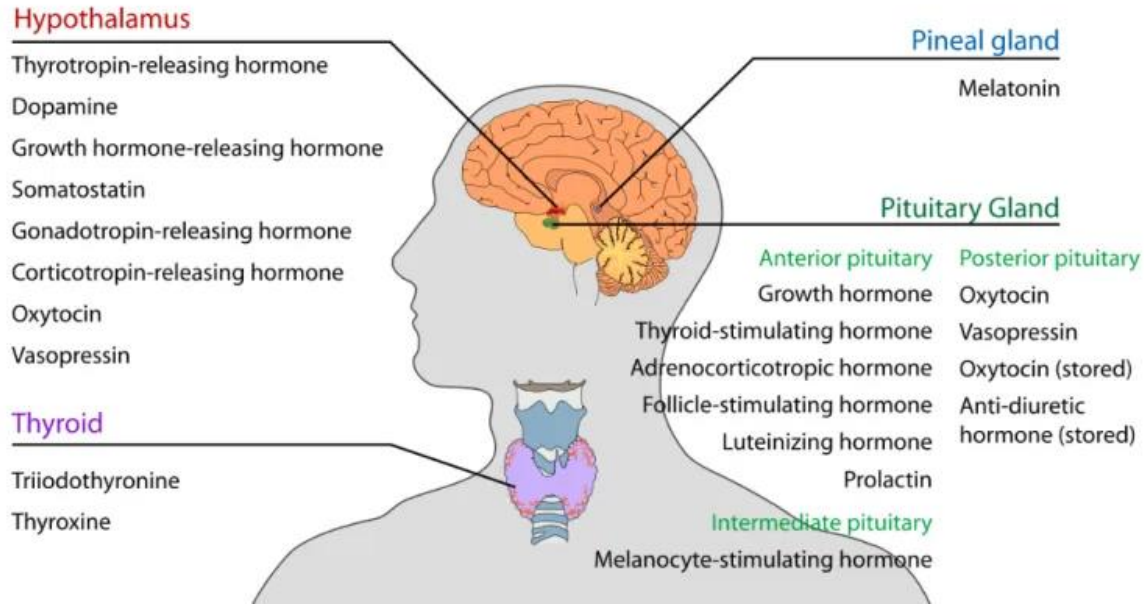
- Part of the lateral nucleus
- Part of suprachiasmatic nucleus
- Anterior nucleus
- Paraventricular nucleus
- Dorsomedial nucleus
- Ventromedial nucleus
- Infundibular nucleus
- Posterior nucleus
- The **nuclei** such as the preoptic nucleus, suprachiasmatic nucleus and the mamillary nuclei are present in both zones of the hypothalamus.



IV. Communications of Hypothalamus

Hypothalamus communicates with the rest of the body via three routes:

- Bloodstream
- Nervous connections
- Endocrine connections



i) Bloodstream connections

Hypothalamus receives blood mainly from the **hypophyseal artery**, a branch of the anterior cerebral artery. All the blood from the hypothalamus is drained into the hypothalamohypophyseal system of veins and distributed to the pituitary gland. From the pituitary gland, the blood is drained via the hypophyseal vein.

ii) Nervous connections

The nervous connections can be divided into afferent and efferent fibers.

Afferent fibers

Hypothalamus receives afferent fibers carrying somatic and visceral sensations as well as from special senses. Following are the important afferents of hypothalamus:

- **Somatic and visceral** afferents via lemniscal afferent fibers and nucleus of tractus solitarius, that reach the hypothalamus via reticular formation
- **Visual** afferents from the optic chiasma reach the suprachiasmatic nucleus
- **Olfactory** afferents are received through medial forebrain bundle
- **Auditory** afferents though not identified completely but are influenced by the hypothalamus
- **Hippocampo-hypothalamic** afferents reach via fornix to mamillary bodies
- **Tegmental** fibers from midbrain

- **Thalamo-hypothalamic** fibers from the midline and dorsomedial nuclei of the thalamus
- **Amygdalo-hypothalamic** fibers from the amygdaloid complex reach the hypothalamus via stria terminalis

Efferent fibers

The efferent connections of hypothalamic nuclei are also complex and numerous. Here, we will mention some important connections.

- **To brain stem and spinal cord**: The hypothalamic nuclei send efferent fibers to nuclei present in the brainstem and spinal cord. In this way, they control the autonomic nervous system.
- **Mammillothalamic Tract:** This tract consists of fibers arising in the mamillary body and terminating in the anterior nucleus of thalamus.
- **Mammillotegmental Tract:** These fibers terminate in the reticular formation, present in the tegmentum of the midbrain.
- **Limbic System:** The nuclei in the hypothalamus also send efferent fibers to the various nuclei of the limbic system.

iii) Endocrine Connections

Hypothalamus uses the bloodstream to communicate with the **pituitary gland**. These connections of the hypothalamus are called the bloodstream or endocrine connections.

The cells of the pituitary gland release hormones in response to the regulating factors or hormones released by the hypothalamus. These regulatory factors reach the pituitary gland via the hypophyseal portal system of veins.

B) Functions of Hypothalamus:

Anterior hypothalamus		*Posterior hypothalamus*	
Nucleus	*Function*	*Nucleus*	*Function*
Paraventricular nucleus	Oxytocin release	Ventromedial nucleus	Satiety and neuroendocrine control
Supraoptic nucleus	Vasopressin release	Lateral hypothalamic area	Thirst and hunger
Medial preoptic area	Bladder contraction, reduce heart rate, and blood pressure	Posterior hypothalamus	Increased blood pressure, pupillary dilation, shivering (cold)
Posterior preoptic and anterior hypothalamic areas	Temperature (heat) regulation, panting, sweating, thyrotropin inhibition	Perifornical nucleus	Hunger, increased blood pressure, rage
		Arcuate nucleus and periventricular zone	Neuroendocrine control, circadian rhythm

Source: Braunstein GD. The hypothalamus .In Melmed S (eds): The Pituitary , 3rd edition . Academic Press , Amsterdam, Elsevier Inc. 2010:303-41.[3]

1.Autonomic Control

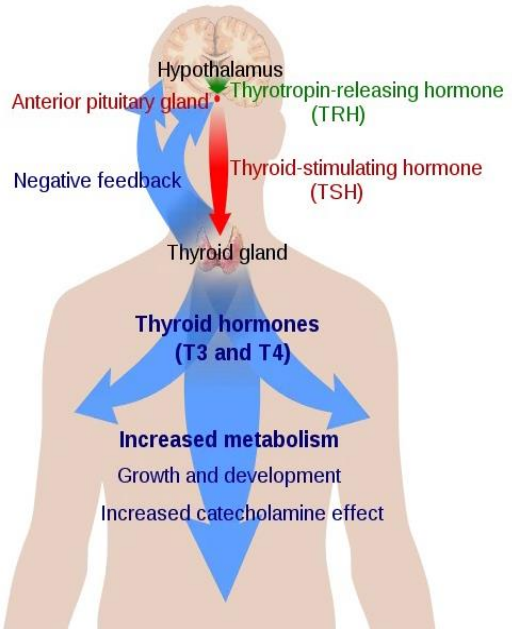
The most important function of the hypothalamus is to integrate the **endocrine system** and the autonomic nervous system. Hypothalamus acts as a higher center for controlling the autonomic functions of the brain stem and spinal cord.

The stimulation of the posterior and lateral nuclei of the hypothalamus has been shown to cause a sympathetic response. On the other hand, the stimulation of the anterior nucleus and the preoptic area influences parasympathetic responses in the body.

2.Endocrine Control

Hypothalamus produces **releasing factors** or **inhibitory factors** for controlling the hormones released by the pituitary gland. These factors include:

- Growth hormone-releasing hormone and inhibiting hormone also called somatostatin
- Prolactin releasing hormone and inhibiting hormone
- Corticotropin-releasing hormone
- Thyrotropin-releasing hormone
- Luteinizing hormone-releasing hormone



These factors promote or inhibit the release of hormones from the **anterior pituitary**. The release of these factors from the hypothalamus is controlled by positive and negative feedback mechanisms depending on the levels of a particular hormone in blood.

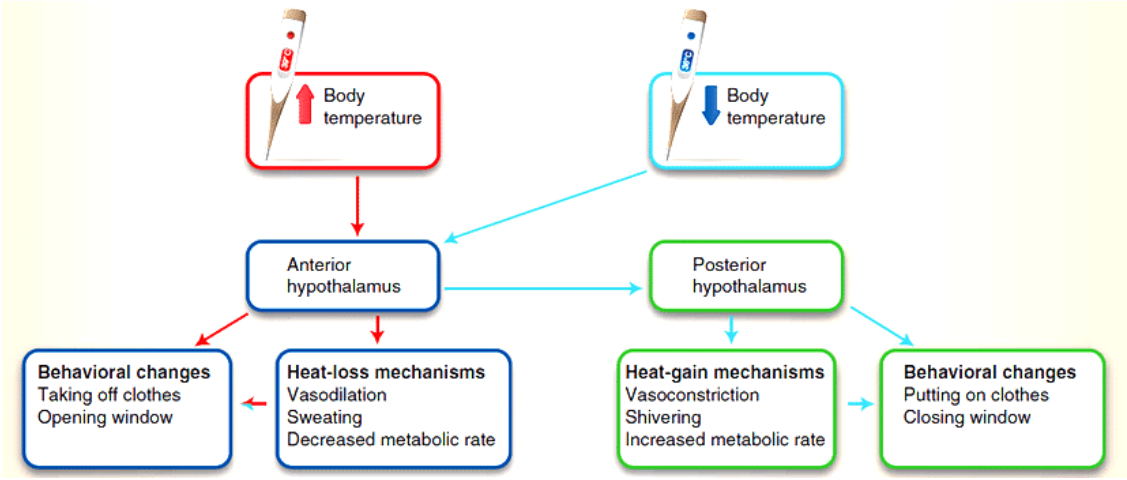
3.Secretion of Hormones

Hypothalamus not only secretes the regulating factors but also secretes two important hormones; **vasopressin** and **oxytocin**. Although these hormones are released from the posterior pituitary, they are actually produced by the neurons in the hypothalamus and are stored in the axonal endings present in the posterior pituitary

4.Temperature Regulation

Temperature regulation is another important function of the hypothalamus.

The anterior part of the hypothalamus controls processes that dissipate heat from the body. Its stimulation causes dilation of blood vessels and sweating, which causes a decrease in body temperature.



Contrary to this, stimulation of the posterior part of the hypothalamus results in vasoconstriction of the skin blood vessels and inhibition of sweating resulting in conservation of body temperature.

5.Controlling Emotions and Behaviour

Being a part of the **limbic system hypothalamus** also controls the emotions and behaviour of a person. It is believed that the hypothalamus integrates all the afferent information from other areas of the brain and brings about the physical expression of emotion.

Stimulation of the lateral area of the hypothalamus is associated with the feelings of rage whereas the stimulation of the medial area results in feelings of passivity.

6.Regulation of Food and Water Intake

Hypothalamus is also the site of the **hunger center** and satiety center in the brain.

The stimulation of the lateral region of the hypothalamus stimulates hunger and results in the intake of food. This region is termed as hunger center.

On the other hand, stimulation of the medial region of the hypothalamus inhibits eating and results in reduced food intake. This is termed as the satiety center of the brain.

7. Potential Problems with the Hypothalamus

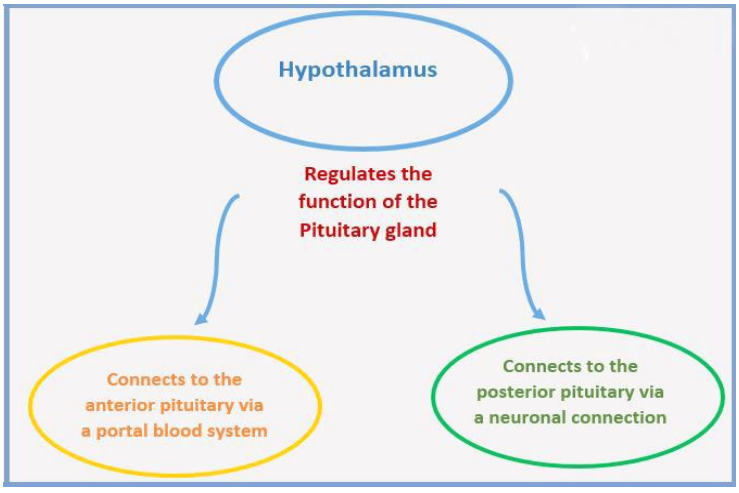
Any lesion of the hypothalamus due to inflammation, tumor, vascular disorder or physical trauma can result in the following clinical disorders.

- Unusually high/low blood pressure
- Fluctuations in body temperature (Hyperthermia or Hypothermia)
- Unintentional weight gain/loss
- Sudden changes in appetite
- Insomnia
- Infertility
- Delayed onset of puberty
- Stunted growth
- Excessive dehydration
- Frequent urination
- Obesity and wasting
- Sexual disorders
- **Emotional disturbances** like weeping, laughter, uncontrollable rage, excessive maniac outbursts and depressive reactions etc.

C) Regulation of Neuroendocrine glands:

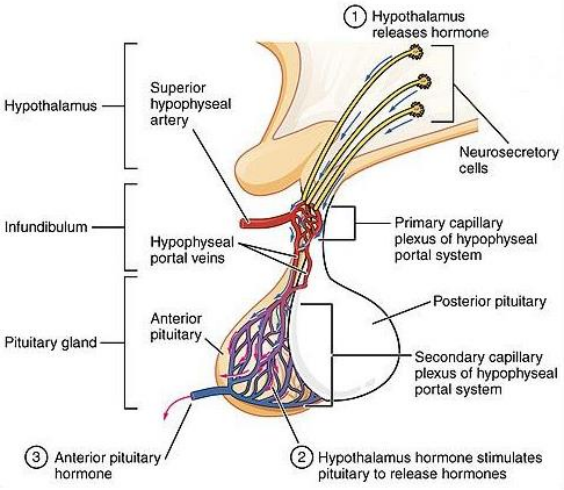
Hormones of the Hypothalamus:

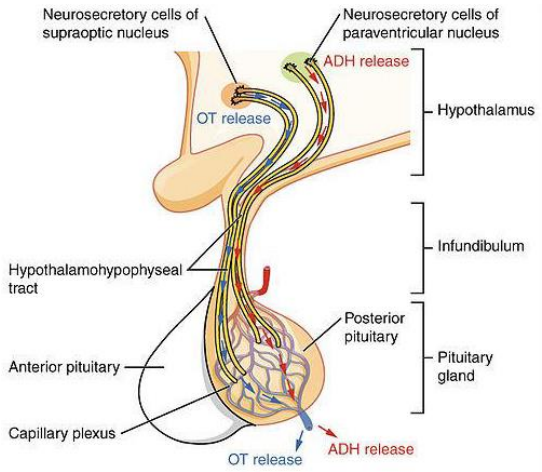
The hypothalamus is highly involved in pituitary gland function. The hypothalamus is connected to the anterior lobe of the pituitary gland by means of a special portal blood system. Moreover, the hypothalamus is directly connected to the posterior lobe of the pituitary gland by means of neurons. Therefore, the hypothalamus regulates the function of the pituitary gland. When it receives a signal from the nervous system, the hypothalamus secretes substances known as neurohormones that start and stop the secretion of pituitary hormones.



Primary hormones secreted by the hypothalamus include:

- **Anti-diuretic hormone (ADH):** This hormone increases water absorption into the blood by the kidneys.
- **Corticotropin-releasing hormone (CRH):** CRH sends a message to the anterior pituitary gland to stimulate the adrenal glands to release corticosteroids, which help regulate metabolism and immune response.
- **Gonadotropin-releasing hormone (GnRH)**: GnRH stimulates the anterior pituitary to release follicle stimulating hormone (FSH) and luteinizing hormone (LH), which work together to ensure normal functioning of the ovaries and testes.





- **Growth hormone-releasing hormone (GHRH)** or **growth hormone-inhibiting hormone (GHIH)** (also known as somatostain): GHRH prompts the anterior pituitary to release growth hormone (GH); GHIH has the opposite effect. In children, GH is essential to maintaining a healthy body composition. In adults, it aids healthy bone and muscle mass and affects fat distribution.
- **Oxytocin**: Oxytocin is involved in a variety of processes, such as orgasm, the ability to trust, body temperature, sleep cycles, and the release of breast milk.
- **Prolactin-releasing hormone (PRH)** or **prolactin-inhibiting hormone (PIH)** (also known as dopamine): PRH prompts the anterior pituitary to stimulate breast milk production through the production of prolactin. Conversely, PIH inhibits prolactin, and thereby, milk production. **Thyrotropin releasing hormone (TRH):** TRH triggers the release of thyroid stimulating hormone (TSH), which stimulates release of thyroid hormones, which regulate metabolism, energy, and growth and development.

D) Feedback Mechanism:

Feedback circuits are at the root of most control mechanisms in physiology, and are particularly prominent in the endocrine system. Hormone secretions in our body are regulated by 2 feedback mechanisms to maintain their homeostasis in the blood: **positive** and **negative**. A feedback loop mechanism is the one in which the secreted end product itself controls its

own production. Instances of positive feedback certainly occur, but negative feedback is much more common.

Negative feedback is seen when the output of a pathway inhibits inputs to the pathway. The heating system in your home is a simple negative feedback circuit. When the furnace produces enough heat to elevate temperature above the set point of the thermostat, the thermostat is triggered and shuts off the furnace (heat is feeding back negatively on the source of heat). When temperature drops back below the set point, negative feedback is gone, and the furnace comes back on.

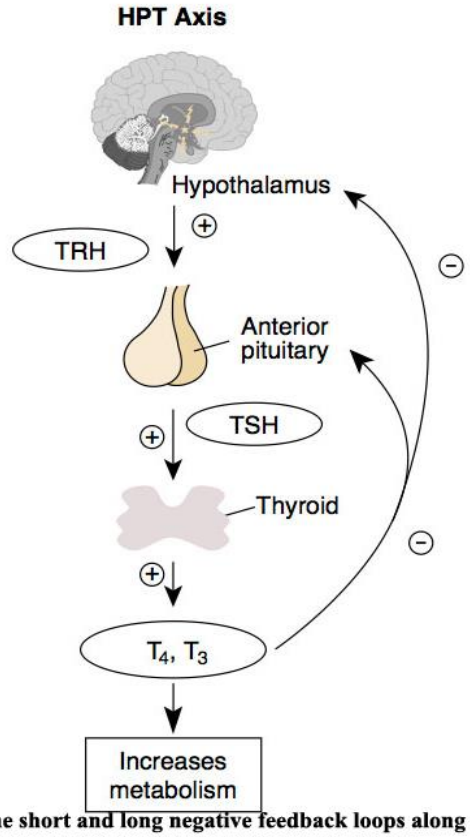


Figure: the short and long negative feedback loops along the hypothalamic-pituitary-thyroid axis (HPT)

Feedback loops are used extensively to regulate secretion of hormones in the hypothalamic-pituitary axis. An important example of a negative feedback loop is seen in control of thyroid hormone secretion. The thyroid hormones thyroxine and triiodothyronine ("T4 and T3") are synthesized and secreted by thyroid glands and affect metabolism throughout the body. The basic mechanisms for control in this system (illustrated to the right) are:

- Neurons in the hypothalamus secrete thyroid releasing hormone (TRH), which stimulates cells in the anterior pituitary to secrete thyroid-stimulating hormone (TSH).
- TSH binds to receptors on epithelial cells in the thyroid gland, stimulating synthesis and secretion of thyroid hormones, which affect probably all cells in the body.
- When blood concentrations of thyroid hormones increase above a certain threshold, TRH-secreting neurons in the hypothalamus are inhibited and stop secreting TRH. *This is an example of "negative feedback".*

Inhibition of TRH secretion leads to shut-off of TSH secretion, which leads to shut-off of thyroid hormone secretion. As thyroid hormone levels decay below the threshold, negative feedback is relieved, TRH secretion starts again, leading to TSH secretion.

In addition to these negative feedback loop, the basal medial hypothalamus also integrates input from other brain centers about changes in the environment, such as a change in temperature, to determine the appropriate level of TSH-RH secretion. This allows the body to regulate secretion of thyroid hormones in response to changes in the environment. Finally, the thyroid also receives input from the autonomic nervous system via parasympathetic and sympathetic fibers to regulate its hormone secretion directly, but the mechanism behind this is not yet well understood.