Hypothalamus - pituitary - adrenal glands

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The hypothalamus is the general director of the hormone system. At every moment, the hypothalamus analyses messages coming from: the brain and different regions of the body.

Afterwards, it performs a number of functions, such as maintaining a stable body temperature, controlling blood pressure, ensuring a fluid balance, and even proper sleep patterns.
Hypothalamus releases hormones at median eminence and sends to anterior pituitary via portal vein.
Function of the releasing and inhibitory hypothalamic hormones

- **Thyrotropin-releasing hormone (TRH)** - causes release of thyroid-stimulating hormone (TSH)
- **Corticotropin-releasing hormone (CRH)** - causes release of ACTH
- **Growth hormone releasing hormone (GHRH)** - causes release of growth hormone, and
- **Growth hormone inhibitory hormone (GHIH)**, which is the same as the hormone somatostatin and which inhibits the release of growth hormone.
Function of the releasing and inhibitory hypothalamic hormones

- **Gonadotropin - releasing hormone (GnRH)**
  - causes release of the two gonadotropic hormones, LH and FSH
- **Prolactin inhibitory hormone (PIH)**,
  - believed to be dopamine - causes inhibition of prolactin release.
- **PRL-releasing factor (PRF)**,
  - believed to be TRH - increases prolactin release
The location of pituitary (hypophysis) relative to brain and hypothalamus
Six very important hormones are secreted by the anterior pituitary:

- Secreted by lactotropes: prolactin (PRL)
- Secreted by thyrotropes: thyroid stimulating hormone (TSH)
- Secreted by gonadotropes: follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
- Secreted by corticotropes: adrenocorticotropic hormone (ACTH)
- Secreted by somatotropes: growth hormone (GH; somatotropin)
Posterior pituitary receives axons from the supraoptic (→ADH) and paraventricular nuclei (→oxytocin).
Growth hormone
(somatotropin)
- **GHRH**, somatostatin (GHIH) and ghrelin (GHIH) and ghrelin control GH release.

- Pancreatic somatostatin has other functions (inhibits hormone secretion by α and β cells).
GH is released in pulses, with a major peak during deep sleep before REM sleep.
Physiology of growth
GH stimulates cartilage and bone growth by:

- increased deposition of protein by the chondrocytic and osteogenic cells that cause bone growth
- increased rate of reproduction of these cells
- the specific effect of converting chondrocytes into osteogenic cells, thus causing specific deposition of new bone.
Direct and indirect effects of GH

- Direct effects are the result of growth hormone binding its receptor on target cells.
- Indirect effects are mediated primarily by an insulin-like growth factor-1 and 2 (IGF-1; IGF-2), hormones that are secreted from the liver and other tissues in response to GH.
**Physiology of growth**

*Growth is affected by:*

- thyroid hormones
- androgens
- estrogens
- glucocorticoids
- insulin
- genetic factors
- adequate nutrition
Physiology of growth - growth periods:

- In humans, there are 2 periods of rapid growth, the first in infancy and the second in late puberty just before growth stops.

- The first period is a continuation of the fetal growth period.

- The second growth spurt is due to an interaction between sex steroids, GH, and IGF-1. 
  
  - Sex hormones $\rightarrow$ ↑amplitude of the spikes of GH secretion $\rightarrow$ ↑IGF-1 $\rightarrow$ ↑growth
Although androgens and estrogens initially stimulate growth, they finally terminate growth by causing the epiphyses to fuse to the long bones.
Metabolic effects of GH
Metabolic effects of GH

- Anabolic
- Increases fat utilisation for energy
- Elevates blood sugar
- Exercise
- Sleep
- Stress

Hypothalamus

GHRH

Somatostatin

Pituitary

GH

Muscle

Bone
(chondrocyte differentiation from fibroblasts)

Adipose tissue

Liver

IGF-1

Direct effects
(antagonizes insulin, synergizes with cortisol, also causes local production of IGF-1)

Indirect effects
(antagonized by cortisol; insulin-like)

Growth promotion (clonal expansion, e.g. chondrocytes)
(bones, soft tissue, gonads, viscera)
GIGANTISM

- excessive production of GH before adolescence
ACROMEGALY - excessive production of GH after adolescence.

Intradental separation and prognathism in a patient with acromegaly.
Acromegaly
The somatopause is directly related to the decline of growth hormone produced by the body during aging.

- **Clinical Signs of the Somatopause:**
  - Weight gain
  - Energy Loss
  - Skin wrinkling
  - Decreasing muscle mass
  - Loss of bone density
  - Increasing body fat (especially around the waist)
GH - youth hormone?

- GH may reverse biological effects of aging
- GH is not recommended for common use in adults
- GH supplementation:
  - GHD
  - AIDS wasting syndrome
  - short bowel syndrome
Other hormones of anterior pituitary:  
ACTH, TSH, FSH, LH, PRL
**ACTH - adrenocorticotropic hormone**

- regulates adrenocortical function
  - stimulates cortisol (glucocorticoid) production by adrenal cortex
  - stimulates aldosterone (mineralocorticoid) production
  - ACTH also exhibits some extraadrenal effects - it has a pigmenting action (MSH activity)
  - CRH, **ACTH** and cortisol secretion exhibit circadian rhythmicity
TSH stimulates the thyroid gland folicles:

- it activates all of the chemical processes that cause T4 production and release by the thyroid gland

- the rate of TSH secretion by anterior pituitary is controlled mainly by the negative feedback effect of T4
FSH functions:

- FSH stimulates early growth of the ovarian follicle
- FSH stimulates spermatogenesis
LH functions:

• LH stimulates ovulation and luteinization

• LH stimulates testosterone secretion
Prolactin
**Hypothalamus**

- Anterior pituitary
- Posterior pituitary

**Prolactin** → ↑ milk synthesis and secretion into alveoli

**Birth** →
- ↓ Prolactin, ↑ neural control (breast mechanorec.)

**Suckling** →
- Hypothal. → ↑ Prolactin 1 hr → ↑ Milk production

Effect weakens over months

- Milk synthesis in alveoli
- Milk secretion from alveoli into ductal system
ADH and oxytocin

- posterior pituitary hormones
Hormones of the posterior pituitary gland

• **Oxytocic hormone:**
  - it causes contraction especially of the uterus and to a lesser degree other smooth muscles of the body
  - it stimulates myoepitelial cells in the breast causing milk ejection
  - it also participates in the process of sperm ejection
"Love hormone" may also help us recognize faces

• hormone associated with trust and social bonding (including pair-bond formation, maternal behavior, sexual behavior)

• helps people recognize familiar human faces
Suckling, baby sounds $\rightarrow$ hypothal $\rightarrow$ \text{↑} oxytocin (paraventricular nucleus) $\rightarrow$ \text{↑} myoepithel. contract $\rightarrow$ milk let-down
Regulation of oxytocin secretion (paraventricular nucleus):

- suckling via stimulation of touch receptors in breast
- distension of female genital tract (during labour)
- pain
- psychological stimuli (baby’s cry, orgasm)
Hormones of the posterior pituitary gland

• **Antidiuretic hormone (ADH; vasopressin):**
  - increases the permeability of the kidney collecting ducts and tubules to water (antidiuretic action)

  - name „vasopressin“ means that it works as a vasoconstrictor
Osmoreceptors in hypothalamus. measure the amount of fluid in your blood at every moment you are alive.
Adrenal glands
Location of adrenal glands

- the outer cortex (80%) releases steroids;
- the inner medulla (20%) releases catecholamines.
The adrenal cortex - three zones
Control of the Secretion of Glucocorticoids by the Adrenal Cortex and of Catecholamines by the Adrenal Medulla

- Hypothalamus
- Corticotropin-releasing hormone (CRH)
- ACTH (adrenocorticotropic hormone)
- Glucocorticoids
- Adrenal cortex (z. fasciculata)
- Adrenal medulla
- Neuron of sympathetic nervous system
- Epinephrine and norepinephrine
The anatomical analogy between cells of adrenal medulla and sympathetic postganglionic neurons

- Postganglionic fiber has effects on one specific effector organ, such as the heart.
- The cells of adrenal medulla may influence the activity of various organs in the body (they secrete hormones to the circulation).
Adrenal catecholamines

The release of AK is carried out by direct connection of nerve fibers from hypothalamus to intermediolateral cells (IML), and then to adrenal medulla.
The metabolic effects of catecholamines (similar to glucagon):

• Increase blood sugar

• Increase rate of lipolysis

• Inhibition of protein degradation (eg. ↓proteolysis in the muscle)
**EPI** raises glycogenolysis in liver/muscle and lipolysis in adipose; elevates blood glucose

**Effects of epinephrine**
The Fight or Flight System
# Adrenergic responses of selected tissues

<table>
<thead>
<tr>
<th>Organ</th>
<th>Receptor</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Heart</td>
<td>Beta-1</td>
<td>Increased inotropy</td>
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<tr>
<td></td>
<td></td>
<td>Increased chronotropy</td>
</tr>
<tr>
<td>Blood vessels</td>
<td>Alpha</td>
<td>Vasoconstriction</td>
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<tr>
<td></td>
<td>Beta-2</td>
<td>Vasodilation</td>
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<tr>
<td>Kidney</td>
<td>Beta</td>
<td>Increased renin release</td>
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<tr>
<td>Gut</td>
<td>Alpha, beta</td>
<td>Decreased motility</td>
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<td></td>
<td>Beta</td>
<td>Increased sphincter tone</td>
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<tr>
<td>Pancreas</td>
<td>Alpha</td>
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<td></td>
<td>Beta</td>
<td>Increased glucagon release</td>
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<tr>
<td>Liver</td>
<td>Alpha, beta</td>
<td>Increased insulin and glucagon release</td>
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<td>Adipose tissue</td>
<td>Beta</td>
<td>Increased glycogenolysis</td>
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<tr>
<td>Skin</td>
<td>Alpha</td>
<td>Increased lipolysis</td>
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<tr>
<td>Bronchioles</td>
<td>Beta-2</td>
<td>Increased sweating</td>
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<tr>
<td>Uterus</td>
<td>Alpha, beta</td>
<td>Bronchodilation</td>
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<td></td>
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<td>Contraction, relaxation</td>
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Adrenal steroids
Adrenal hormones are derivatives of cholesterol
Glucocorticoids

Cortisol
Hypothalamic - pituitary adrenal axis

Corticotropes in hypothalamus → CRH → portal → pituitary → ACTH → adrenal cortex → cortisol
Describe changes in human body that occur during stress
Metabolic effects of cortisol

- Catabolic
- Increase of lipolysis
- Increase blood sugar
The effects of cortisol on skeletal muscle

- Plasma
- Cortisol
- Amino acids
- Muscle protein

Cortisol -> Amino acids (+)
Amino acids -> Muscle protein (+)
Cortisol -> Muscle protein (-)
Cortisol accelerates liver urea cycle and amino acid conversion to glucose.
Summary of effects of cortisol on metabolism:

**LIVER:**
- ↑ gluconeogenesis, and glycogen synthesis

**SKELETAL MUSCLE:**
- ↓ protein synthesis;
- ↑ protein degradation;
- ↓ glucose uptake;

**ADIPOSE TISSUE:**
- ↓ glucose uptake;
- ↑ lipid mobilization
Cushing’s syndrome - long lasting increase in plasma corticoids
Cushing’s syndrome

- skin and subdermal tissues are thin, and muscles are poorly developed
- wounds heal poorly and minor trauma causes bruises and ecchymoses
- very severe osteoporosis
- facial hair and acne
- obesity with “buffalo torso” and “moon face”
- adrenal diabetes
- 80% of patients have hypertension
- mental symptoms and sleep disorders
- reduced sex drive and fertility in man
- irregular or stopped menstrual cycles in women
Obesity with "buffalo torso"

Acne
Cushing syndrome
Mineralocorticoids

Aldosterone
(z. glomerulosa)

If the aldosterone of ten million people were pooled together, only one gram of the hormone would result.
Effects of mineralocorticoids:

- Na$^+$ reabsorption in the collecting tubules
- K$^+$ and H$^+$ loss with urine
- Reabsorption of Na$^+$ and the secretion of K$^+$ by salivary and sweat glands
- High aldosterone: hypokalemia, muscle weakness and mild alkalosis
 Decreased kidney blood pressure (↓ ECF) → renin → converts angiotensinogen to angiotensin I. Lung ACE converts angiotensin I to II → angiotensin II stimulates aldosterone release.

Aldosterone causes Na⁺ and H₂O retention, increase in ECF and finally inhibition of the primary stimuli.
Adrenal androgens
Effects of adrenal androgens and estrogens

- Androgens are the hormones responsible for masculinization, and they also promote protein anabolism and growth.
- They cause epiphyses to fuse in the long bones, thus eventually stopping growth.
- They slightly increase $\text{Na}^+$, $\text{K}^+$, $\text{H}_2\text{O}$, $\text{Ca}^{++}$, sulfate and phosphate retention and they increase the size of the kidneys.
The androgenital syndrome:

- **typical masculine characteristics:**
- much deeper voice
- occasionally baldness
- masculine distribution of hair on the body
- masculine features
- salt loosing form and hypertensive form
The androgenital syndrome:

- Genitals of female baby masculinized by prenatal hypersecretion of adrenal androgens
Adrenal insufficiency

Loss of glucocorticoid and mineralocorticoid action – predict the typical findings
Addison's disease

- Low plasma $\text{Na}^+$, high plasma $\text{K}^+$
- Inability to produce concentrated urine by the kidneys $\rightarrow$ excessive urination
- Vomiting, loss of appetite, anorexia, dehydration
- Low blood pressure
- Muscle weakness, fatigue
- Low blood sugar
- Excess pigmentation of skin in some patients