The ENDOCRINE SYSTEM
Orchestration & Regulation

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COMMUNICATION SYSTEM
Endocrine System, Nervous System

1. Communication
2. Response coordination
3. Stress management

- The Nervous System – FAST RESPONSE, neurotransmitters, short lived
- The Endocrine System – SLOW RESPONSE, bloodstream, longer lasting

- They nervous and endocrine systems work together to detect external and internal signals, transmit and integrate information, and maintain homeostasis..

The endocrine system is a series of glands that produce and secrete hormones that the body uses for a wide range of functions:

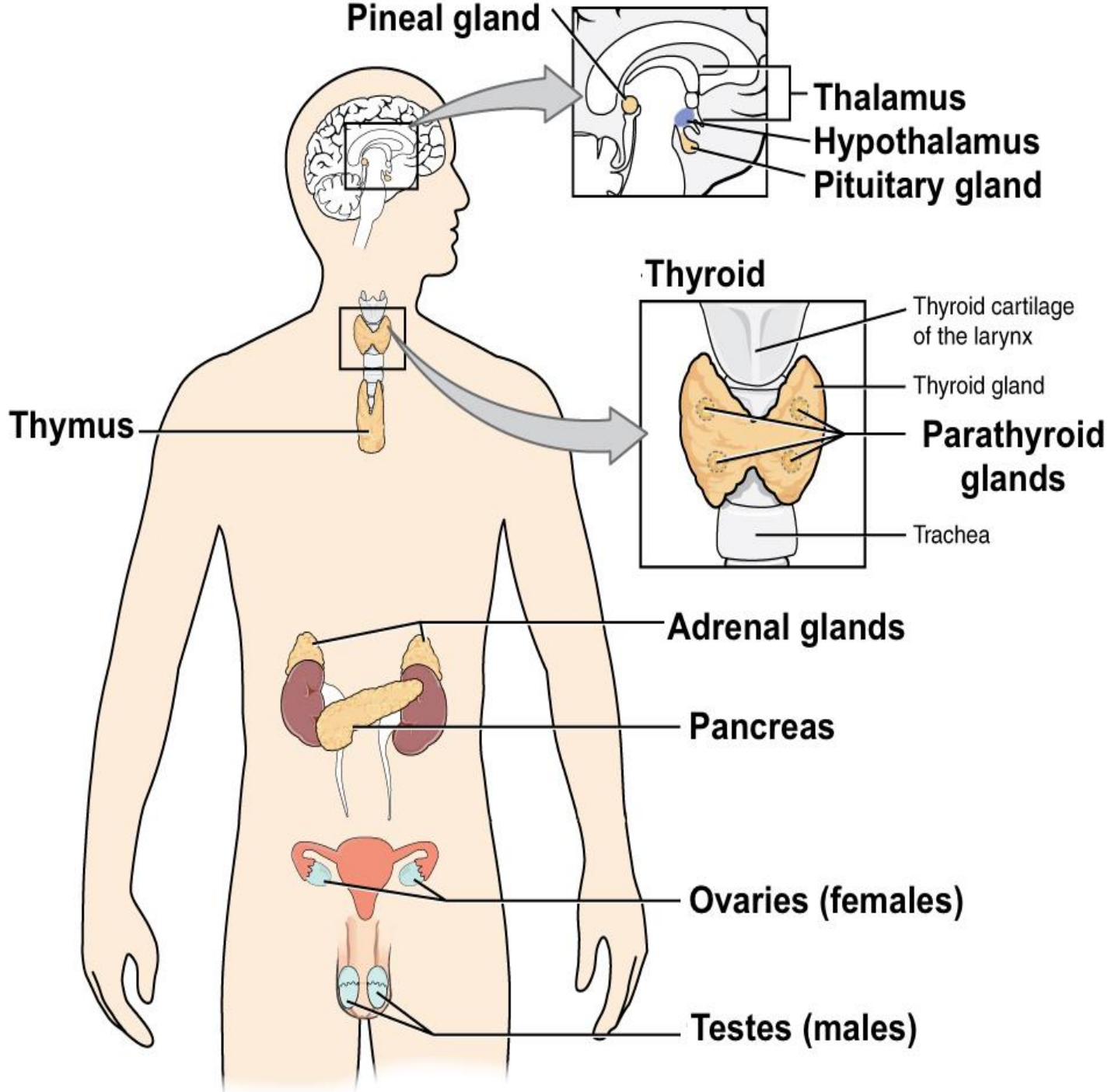
1. Orchestration and Regulation – hypothalamus, pituitary, pineal glands in brain

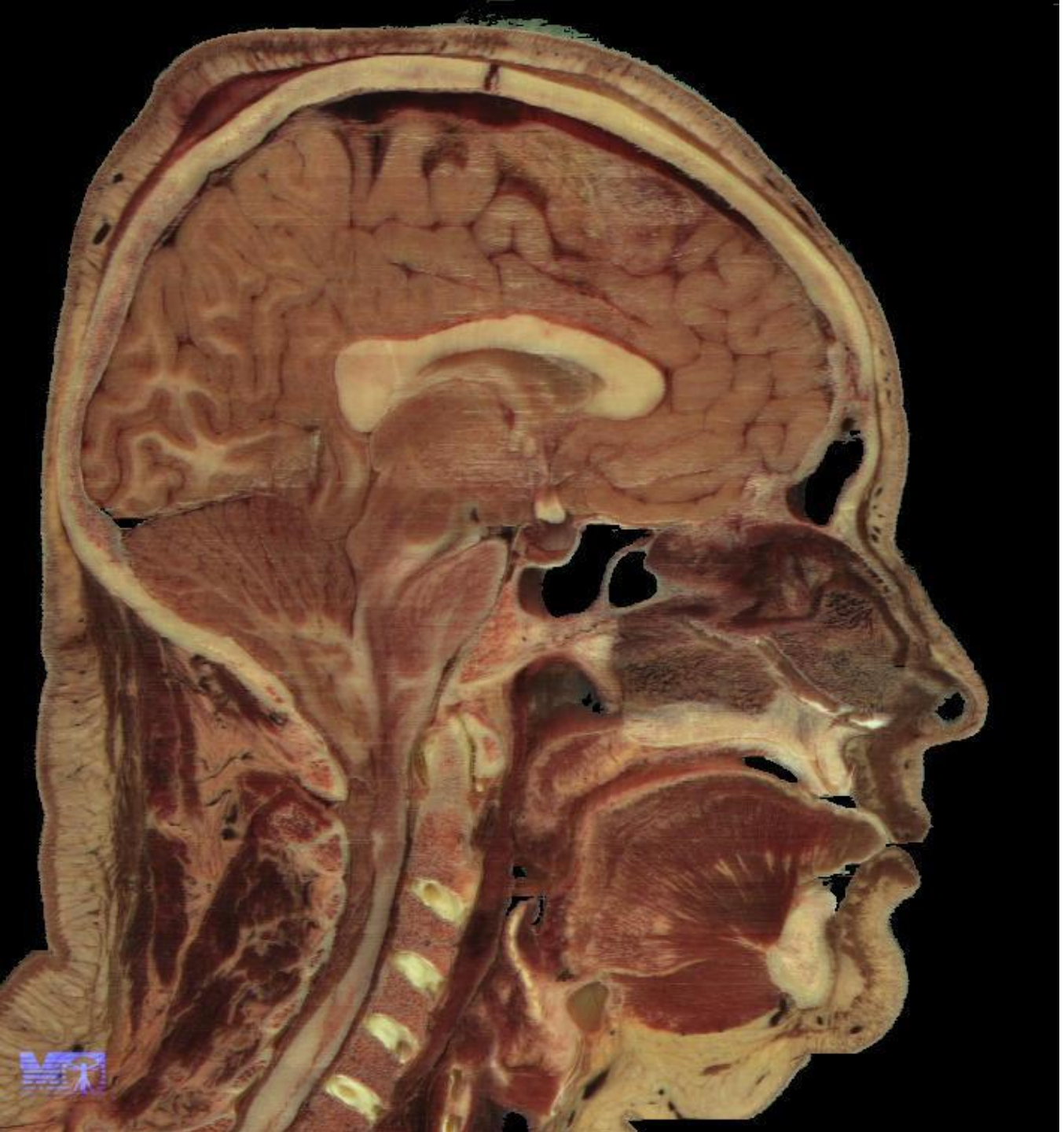
2. Metabolic Rate – thyroid, parathyroid, thymus – (skin and kidneys for Vit D activity)

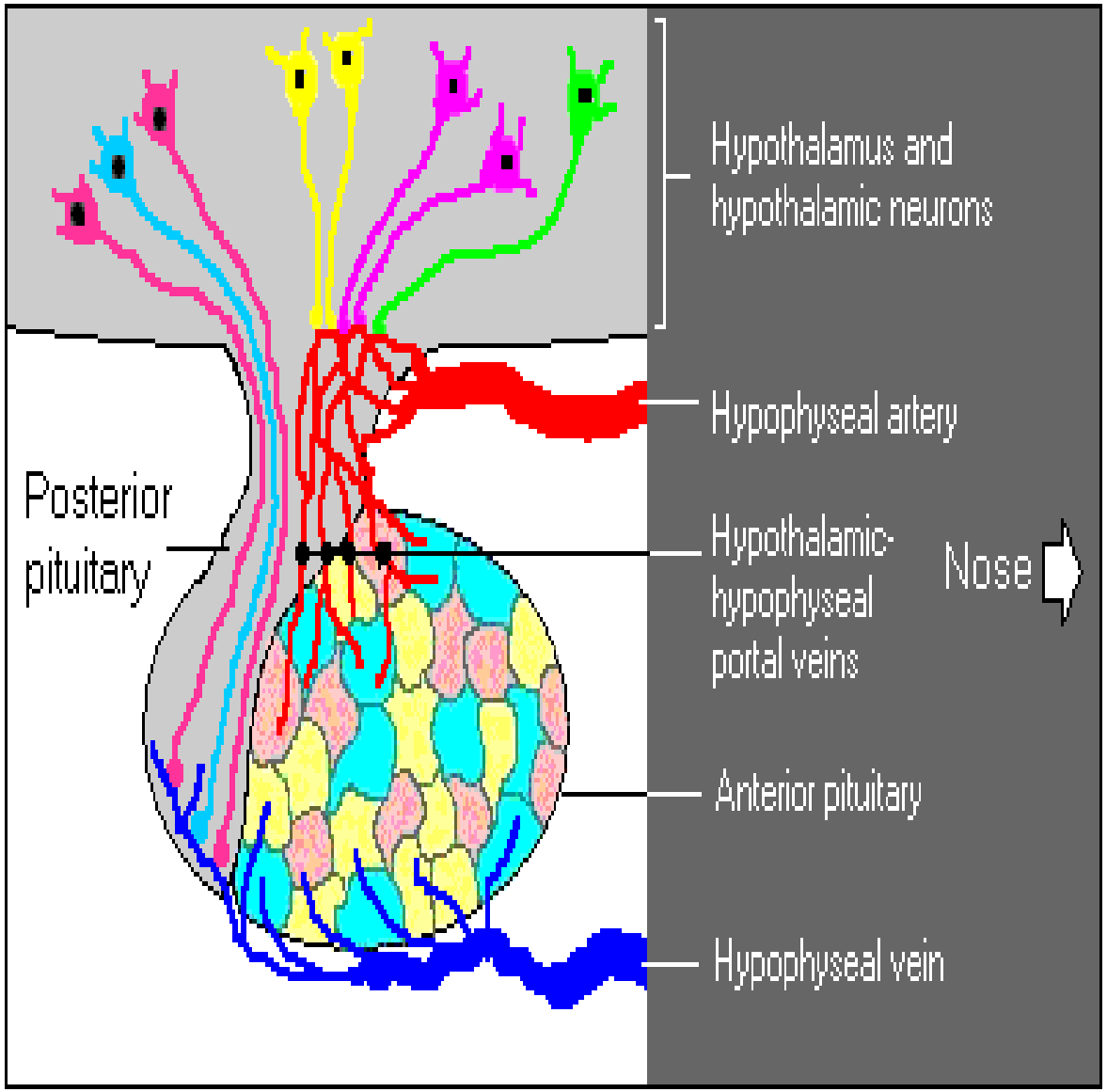
3. Energy Metabolism – pancreas, liver, adrenal cortex, fat cells, stomach, intestines

4. Adrenal function – adrenal glands, kidneys

5. Reproduction – female ovaries and uterus, male testes and prostate, breast tissue

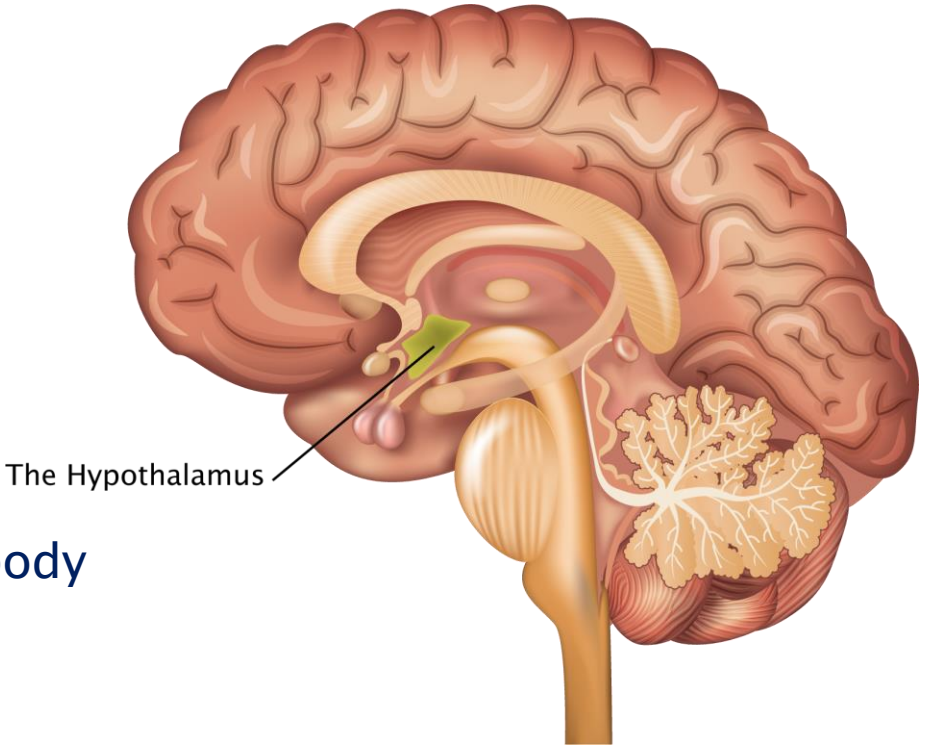

Pineal gland
Thalamus
Hypothalamus
Pituitary gland
Thyroid
Thyroid cartilage of the larynx
Thyroid gland
Parathyroid glands
Trachea
Thymus
Adrenal glands
Pancreas
Ovaries (females)
Testes (males)




Hypothalamus and hypothalamic neurons
Hypophyseal artery
Posterior pituitary
Hypothalamic-hypophyseal portal veins
Nose
Anterior pituitary
Hypophyseal vein

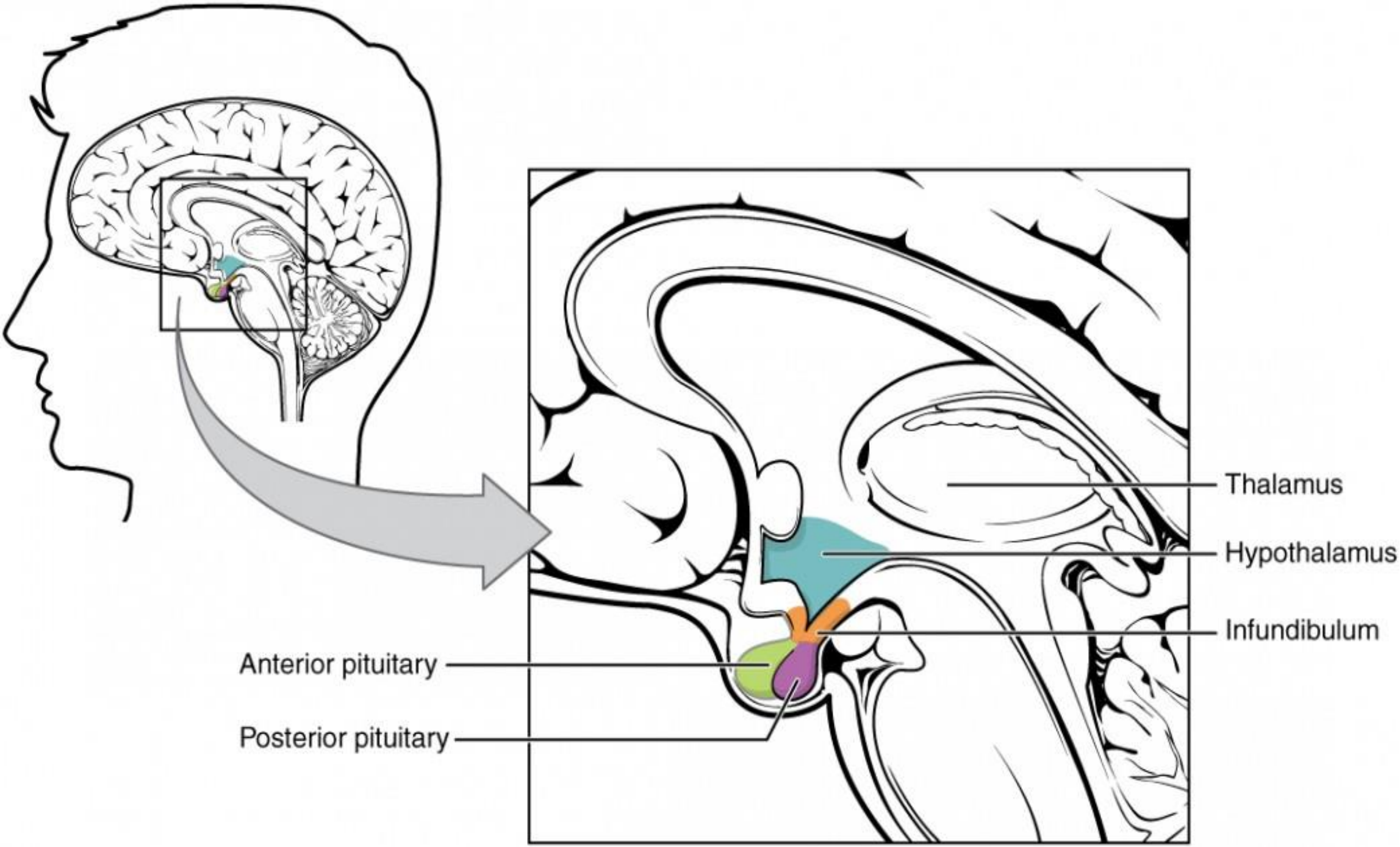
1. Orchestration and Regulation

Hypothalamus



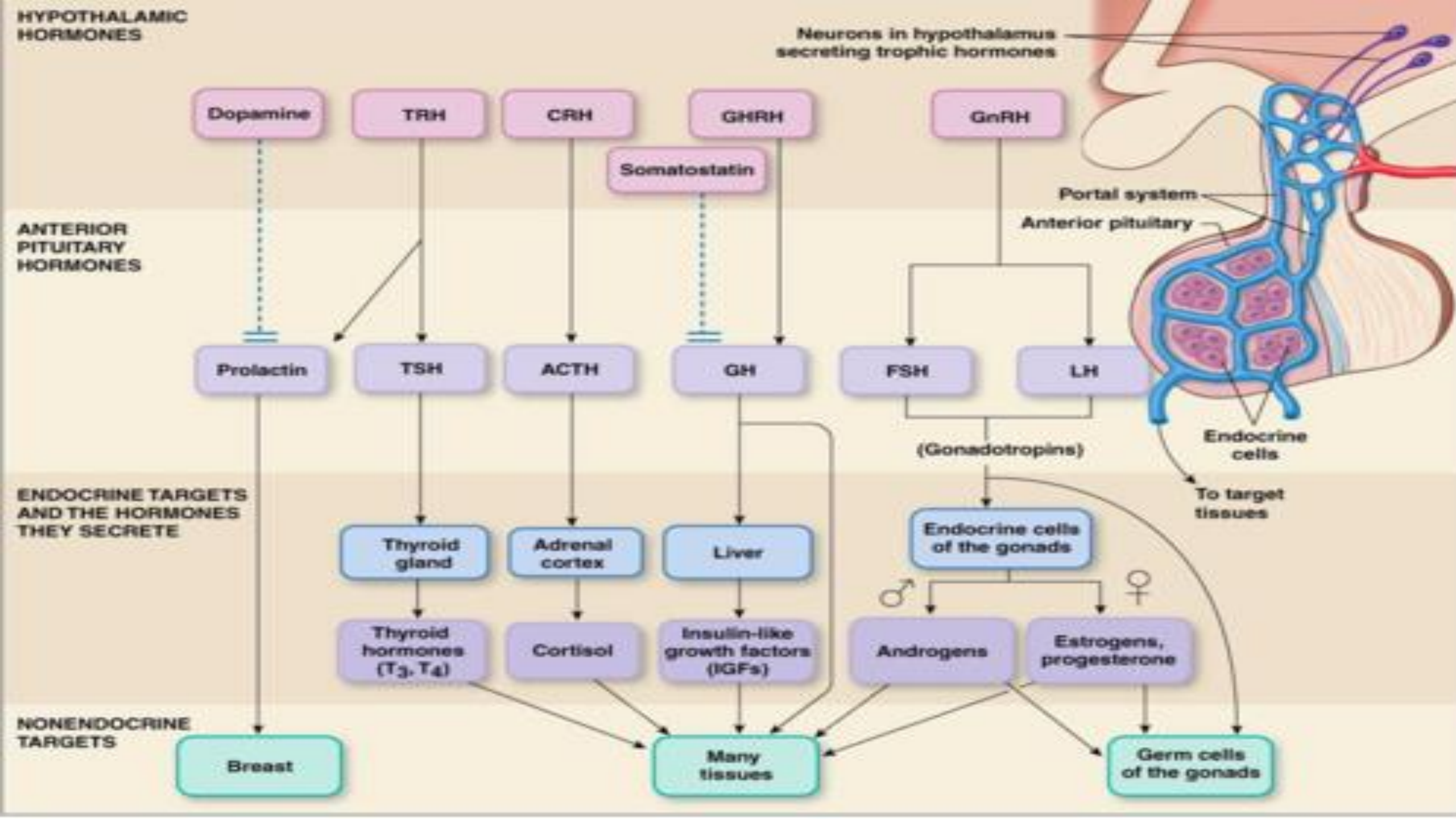
- Portion of the brain that maintains body's homeostasis
- Link between the endocrine and nervous systems
- produces releasing and inhibiting hormones, which stop and start the production of other hormones throughout the body
- Stimulates or inhibits key bodily processes:

  - Heart rate and blood pressure
  - Body temperature
  - Fluid and electrolyte balance, including thirst
  - Appetite and body weight
  - Glandular secretions of the stomach and intestines
  - Sleep cycles
  - Production of substances that influence the pituitary gland to release hormones


Thalamus
Hypothalamus
Infundibulum
Anterior pituitary
Posterior pituitary

Relationship between Hypothalamus releasing hormones and hormones they stimulate

Releasing Hormone	Stimulated Hormone
Thyrotrophin-releasing hormone (TRH)	Stimulates the release of thyroid-stimulating hormone (**TSH**) and **PROLACTIN** from the anterior pituitary. Kidney disease, hypothyroidism, certain Rx can lead to elevated prolactin, which decreases testosterone
Corticotropin-releasing hormone (CRH)	Stimulates ACTH release from pituitary
Gonadotropin-releasing hormone (GnRH)	Stimulates release of LH and FSH from pituitary
Growth hormone-releasing hormone (GHRH)	Stimulates secretion of growth hormone from pituitary, somatotropin. Control lipids, proteins and carbohydrates metabolism.
Somatostatin	Inhibit secretion of GH from anterior pituitary and TSH. In addition, somatostatin is produced in the pancreas and inhibits the secretion of


HYPOTHALAMIC HORMONES
Neurons in hypothalamus secreting trophic hormones
Dopamine
TRH
CRH
GHRH
GnRH
Somatostatin
Portal system
Anterior pituitary
ANTERIOR PITUITARY HORMONES
Prolactin
TSH
ACTH
GH
FSH
LH
(Gonadotropins)
Endocrine cells
To target tissues
ENDOCRINE TARGETS AND THE HORMONES THEY SECRETE
Thyroid gland
Adrenal cortex
Liver
Endocrine cells of the gonads
♂
♀
Thyroid hormones (T_3, T_4)
Cortisol
Insulin-like growth factors (IGFs)
Androgens
Estrogens, progesterone
NONENDOCRINE TARGETS
Breast
Many tissues
Germ cells of the gonads

SIGNAL TRANSDUCTION CASCADE

(process how signal is transmitted through a cell)

1st vs 2nd MESSENGER MOLECULES

First messengers are extracellular ligands/factors, often **hormones or neurotransmitters**, such as epinephrine, growth hormone, and serotonin. Earl Wilbur Sutherland Jr., discovered second messengers, for which he won the 1971 **Nobel Prize.**

Second messenger molecules include **cyclic AMP**, cyclic GMP, inositol triphosphate, diacylglycerol, and calcium.

Sutherland discovery - epinephrine alone not successful, but had to trigger a second messenger, cyclic AMP, for the liver to convert glycogen to glucose

Cyclic AMP (Cyclic adenosine monophosphate)

Metabolism, gene regulation, regulation of neurotransmitter synthesis, growth factors, and immune function are some examples of the numerous biological processes that utilize cAMP
Understanding the cAMP pathway gives rise to therapeutic possibilities within the signal transduction system to fight against diseases such as cancer, diabetes, heart failure, inflammation, neurological disorders, myocardial atrophy, and mood disorders

The chief role of cyclic AMP in several tissues is to facilitate or promote the **mobilization of glucose and fatty acid reserves**. In the liver, glucagon and the catecholamines cause an increase in the intracellular level of cyclic AMP by stimulating adenyl cyclase.

SOMATOSTATIN - somatotropin release-inhibiting factor (SRIF)

While there is no data relating to under-production of somatostatin, there are documented cases of OVER-PRODUCTION of somatostatin referred to as **SOMATOSTATINOMA**.

Somatostatin produces predominantly neuroendocrine inhibitory effects across multiple systems. It is known to inhibit GI, endocrine, exocrine, pancreatic, and pituitary secretions, as well as modify neurotransmission and memory formation in the CNS.

Somatostatin acts by inhibiting the cyclic 3',5'-adenosine monophosphate (cAMP)/protein kinase A pathway, cAMP response element-binding protein (CREB) phosphorylation, and CREB transcription potency. Mol Endocrinol.

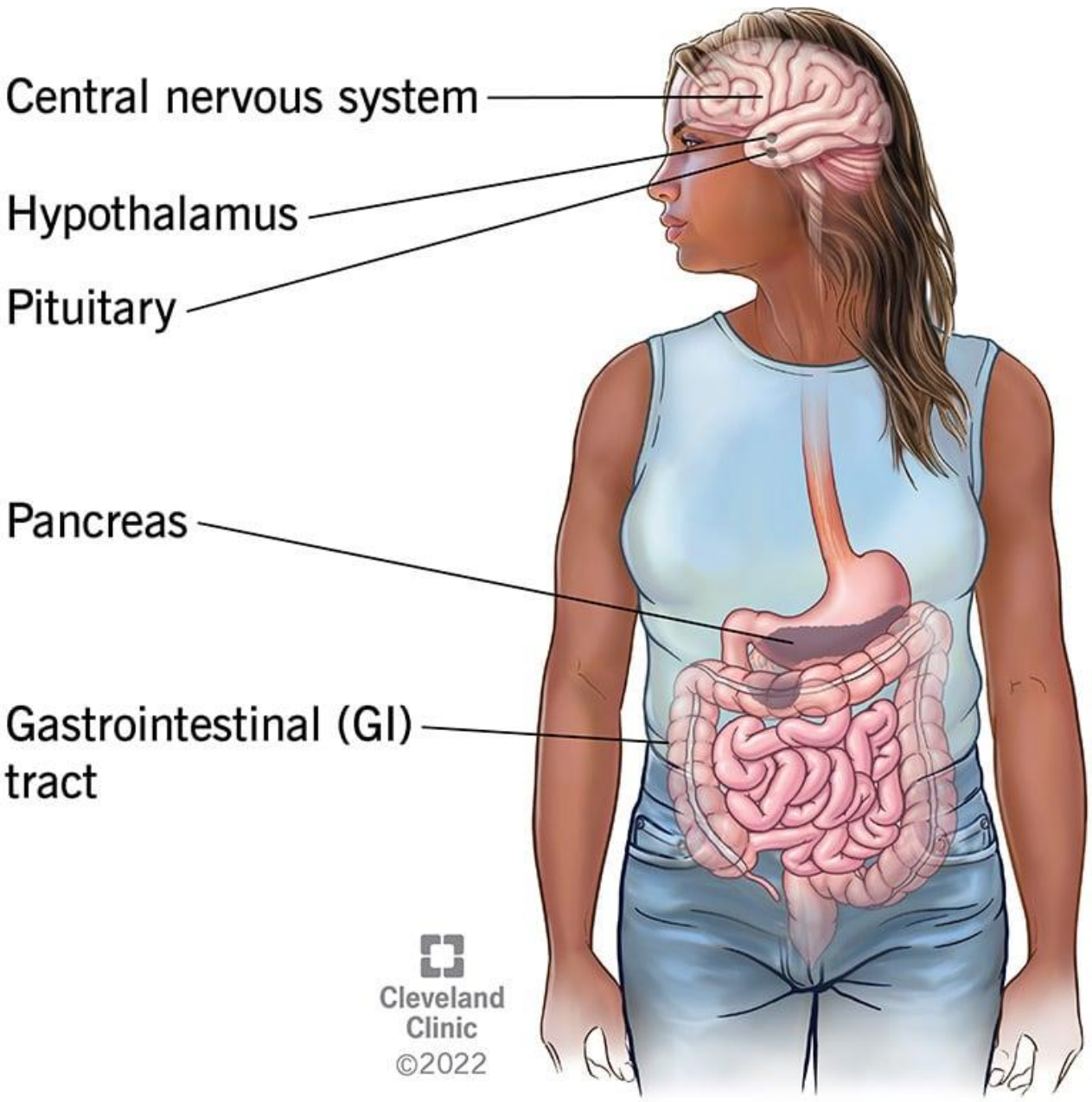
https://pubmed.ncbi.nlm.nih.gov/9178746/#:~:text=Somatostatin%20acts%20by%20inhibiting%20the%20cyclic%203'%2C5'%2Dadenosine,Mol%20Endocrinol

SOMATOSTATIN

Somatostatin, an inhibitor of ACTH secretion, decreases cytosolic free calcium and voltage-dependent calcium current in a pituitary cell line. J Neurosci.
https://pubmed.ncbi.nlm.nih.gov/2430073/#:~:text=pituitary%20cell%20line_,Somatostatin%2C%20an%20inhibitor%20of%20ACTH%20secretion%2C%20decreases%20cytosolic%20free%20calcium,J%20Neurosci

Somatostatin (SST) potently inhibits insulin and glucagon release from pancreatic islets. Endicronology
https://pubmed.ncbi.nlm.nih.gov/10614629/#:~:text=Somatostatin%20(SST)%20potently%20inhibits%20insulin,to%20regulate%20pancreatic%20endocrine%20function

Somatostatin



Glucose stimulates somatostatin secretion in pancreatic δ-cells by cAMP-dependent intracellular Ca^{2+} release

- Somatostatin secretion from pancreatic islet δ-cells is stimulated by **elevated glucose levels**.
- In pancreas, somatostatin is powerful intra-islet inhibitor of insulin glucagon secretion, gastrin and pancreatic enzymes. In GI tract, somatostatin reduces gastric secretion.
- Somatostatin receptor antagonists could restore counterregulatory glucagon secretion.
- Forskolin has an effect on cytoplasmic cAMP levels in pancreatic islet cells
- GlucoResolve (Biotics Research) contains Forskolin

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6719402/#:~:text=Somatostatin%20secretion%20from%20pancreatic%20islet,have%20only%20partially%20been%20elucidated

HYPOTHALAMUS – EMOTIONS

The hypothalamus also plays an important role in emotion.
Lateral parts of the hypothalamus is involved in emotions such as pleasure and rage.
The median part is associated with aversion, displeasure, and a tendency to uncontrollable and loud laughing.
The hypothalamus has more to do with the expression (symptomatic manifestations) of emotions than with the genesis of the affective states.

How can I reset my hypothalamus naturally?

Foods rich in **polyphenols** may help improve the functioning of the hypothalamus. Several vitamins, including vitamin **C**, **thiamine**, and vitamin **B12**, may also aid the functioning of the hypothalamus.

Somatostatin vs Dopamine balance

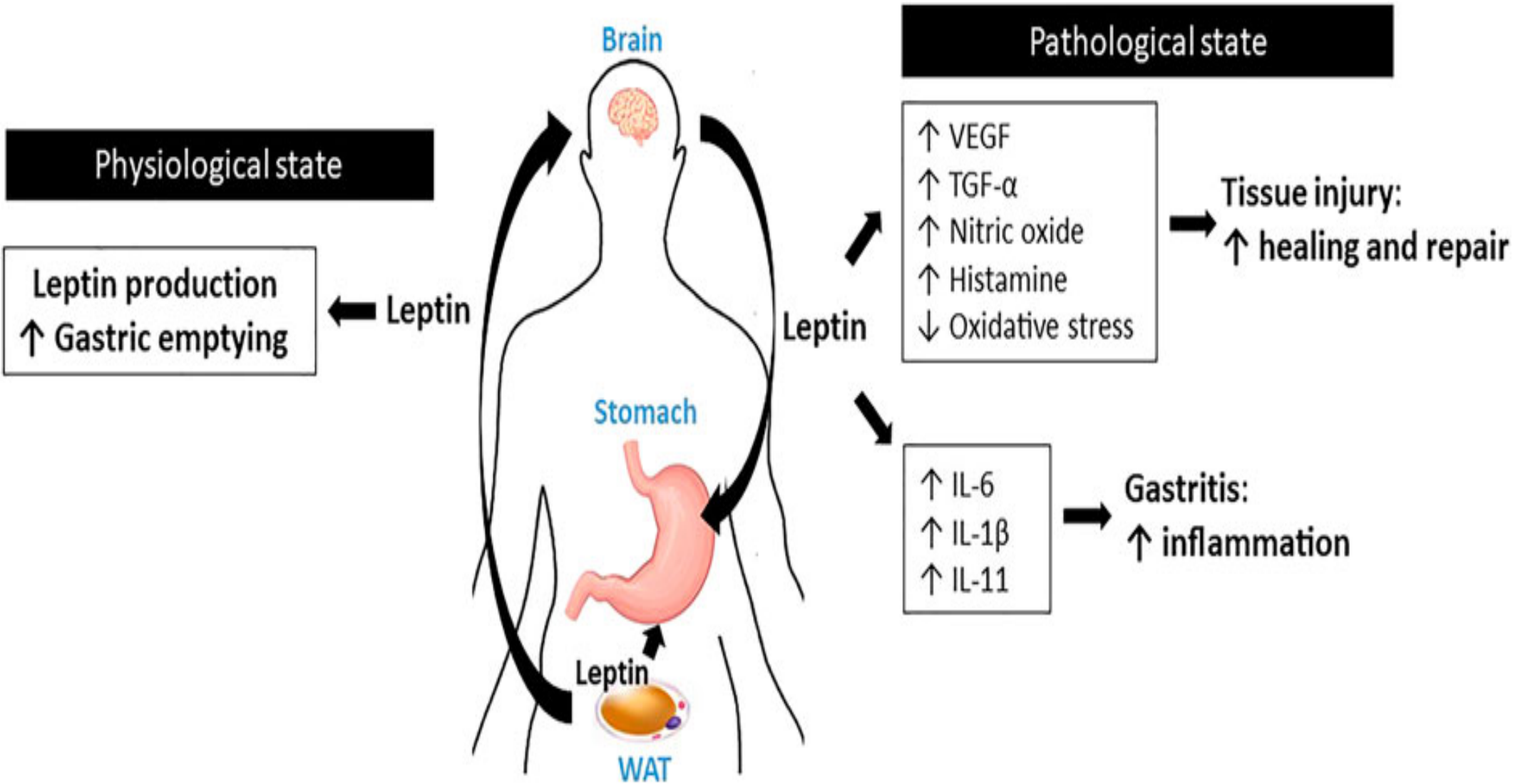
Dopaminergic suppression of pancreatic somatostatin secretion

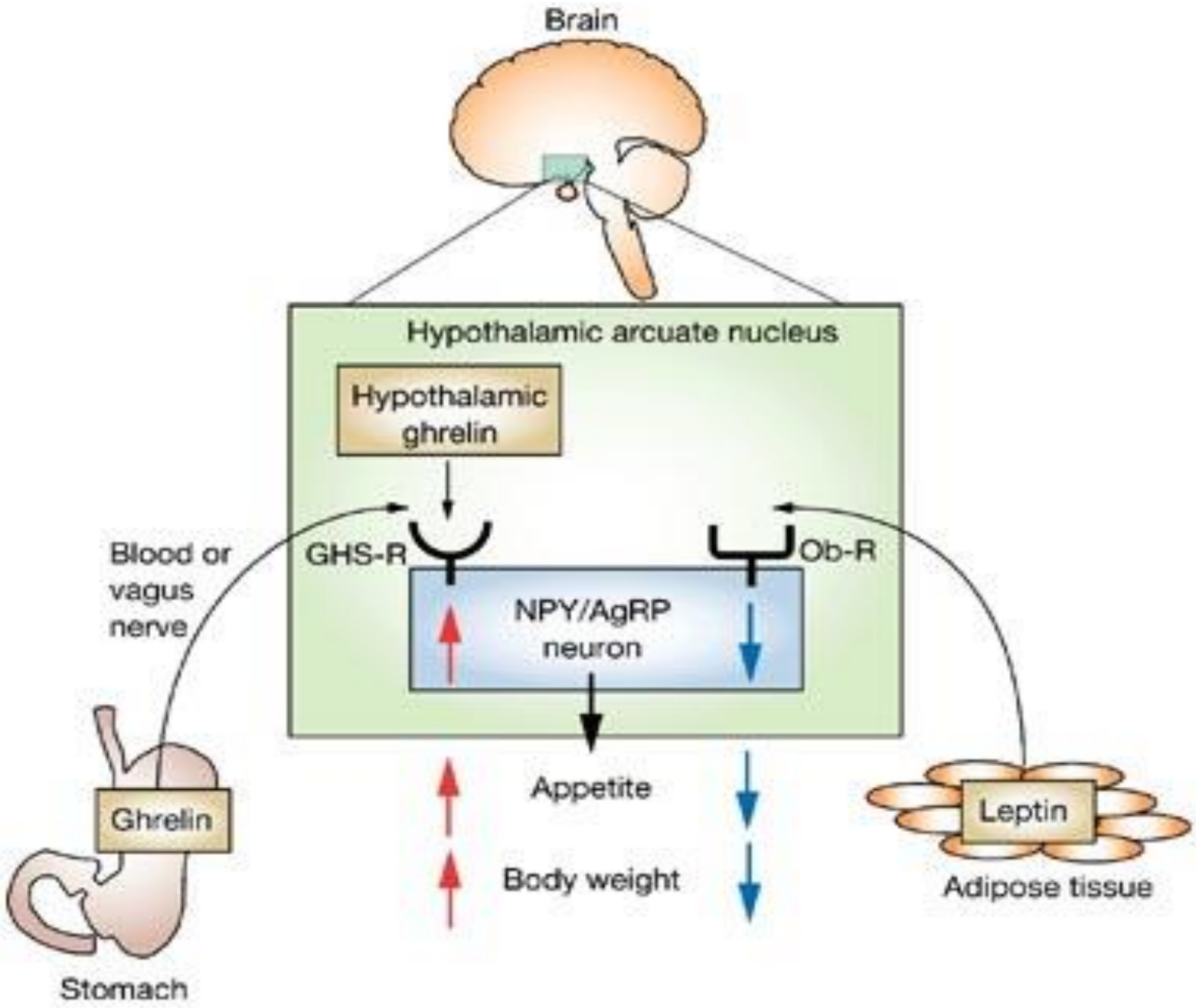
Dopamine regulates pancreatic glucagon and insulin secretion via adrenergic and dopaminergic receptors Translational Psychiatry

https://www.nature.com/articles/s41398-020-01171-z

Dopaminergic Regulation of Insulin Secretion from the Pancreatic Islet Molecular Endicronology

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3725340/#:~:text=Exogenous%20dopamine%20inhibits%20insulin%20secretion,the%20regulation%20of%20insulin%20secretion


Physiological state
Leptin production
↑ Gastric emptying
Leptin
Brain
Stomach
Leptin
WAT
Leptin
Pathological state
↑ VEGF
↑ TGF-α
↑ Nitric oxide
↑ Histamine
↓ Oxidative stress
Tissue injury:
↑ healing and repair
↑ IL-6
↑ IL-1β
↑ IL-11
Gastritis:
↑ inflammation


Brain
Hypothalamic arcuate nucleus
Hypothalamic ghrelin
GHS-R
Ob-R
NPY/AgRP neuron
Blood or vagus nerve
Ghrelin
Stomach
Appetite
Body weight
Leptin
Adipose tissue

How does leptin work?

Leptin is made by adipose tissue (aka fat) and is secreted into the circulatory system, where it travels to the hypothalamus. Leptin tells the hypothalamus that we have enough fat, so we can eat less or stop eating. Leptin may also increase metabolism, although there is conflicting research on this point.

Generally, the more fat you have, the more leptin you make; the less food you'll eat; and the higher your metabolic rate.

Conversely, the less fat you have, the less leptin you have, and the hungrier you'll be.

Basically, for weight loss — the more leptin the better.

Leptin resistance vicious cycle.

1. Eat more, gain body fat.
2. More body fat means more leptin in fat cells.
3. Too much fat means that proper leptin signaling is disrupted.
4. The brain thinks you're starving, which makes you want to eat more.
5. You get fatter. And hungrier.
6. You eat more. Gain more fat.

Leptin resistance

Similar to **insulin resistance** (they share common signaling pathways). Insulin resistance occurs - lots of insulin being produced, but the body and brain have stopped "listening" to insulin's effects. Both occur in **obese people**

- Obese men - higher insulin levels
- Obese women - higher leptin levels

Fructose seems to induce leptin resistance (NAFLD).

- ❑ Sleep
- ❑ Exercise
- ❑ Check Diabetes/Sugar Balance protocol
- ❑ Check liver protocol

1. Orchestration and Regulation cont.

Pituitary Gland

- functions as directed by the Hypothalamus
- Endocrine system's "Master gland" – hormones help regulate the functions of other endocrine glands
- two parts:
  - Anterior lobe

    The anterior lobe releases hormones upon receiving releasing or inhibiting hormones from the hypothalamus. These hypothalamic hormones tell the anterior lobe whether to release more of a specific hormone or stop production of the hormone.

  - Posterior lobe

    The posterior lobe contains the ends of nerve cells coming from the hypothalamus. The hypothalamus sends hormones directly to the posterior lobe via these nerves, and then the pituitary gland releases them.

Seven Stimulating Hormones of the Anterior Pituitary

Stimulating Hormone	Description
Thyroid stimulating hormone (TSH)	Stimulates the thyroid to produce and secrete thyroid hormones
Follicle-stimulating hormone (FSH)	Promotes follicular development and estrogen synthesis in ovaries; sperm maturation-testes
Luteinizing hormone (LH)	Stimulates ovulation, formation of corpus luteum, estrogen and progesterone synthesis in ovaries. Stimulates testosterone in testes.
Adrenocorticotropic hormone (ACTH)	Stimulates synthesis and secretion of adrenal cortical hormones (cortisol, androgens, aldosterone).
Melanocyte-stimulating hormone (MSH)	Stimulates melanin synthesis.
Growth hormone (GH) or somatotropin, also known as human growth hormone (hGH or HGH)	Stimulates growth, cell reproduction, cell regeneration. Goes directly to long bones and the big muscles to stimulate growth. GH also stimulates production of IGF-1 (**Insulin-like growth factor 1**) and increases the

ACTH – ADRENAL GLANDS

CORTEX

- Cortisol – increases blood glucose, suppresses immune system, stress response
- Aldosterone – Na reabsorption. Travels to kidneys, instructs to keep Na. Water follows Na – more volume of blood, increases blood pressure. Maintains HYDRATION.
- Androgens

MEDULLA

- Noradrenaline
- Adrenaline

GH, GONADOTROPINS

GH

- Growth hormone – big bones and muscles

PROLACTIN

- Milk production, not ejection, that's OXYTOCIN

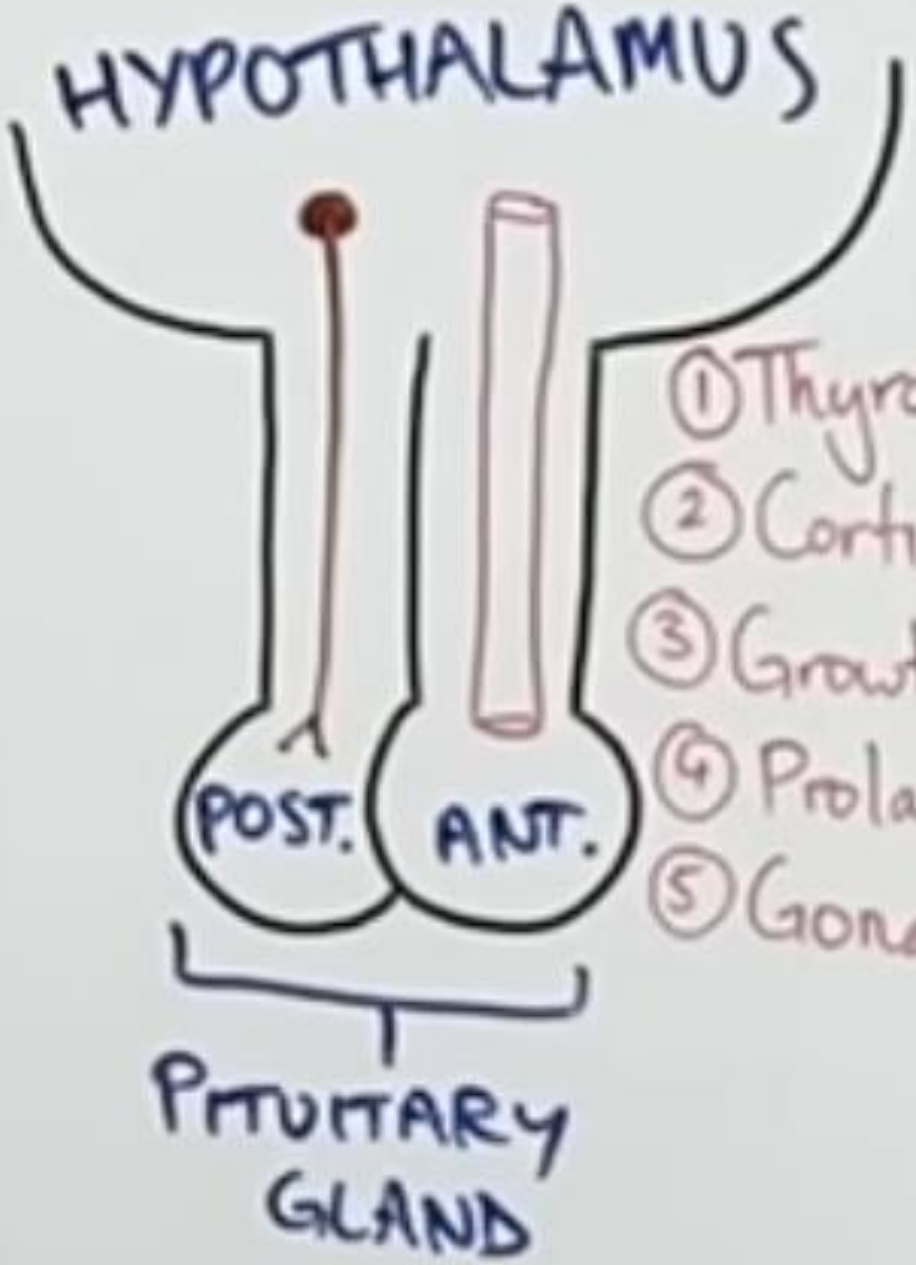
GONADOTROPINS

FEMALE

- LH – ovulation – progesterone
- FSH – follicle stimulation – estrogen. UTERUS PREPARATION

MALE

- LH – Leydig – testosterone
- FSH – Sertoli Cells – Androgen Bonding Protein. SPERM PRODUCTION



1. Thyrotropin rel. h.
2. Corticotropin rel. h.
3. Growth hormone rel. h.
4. Prolactin rel. h.
5. Gonadotropin rel. h.

Two Pass-through Hormones of the Posterior Pituitary

Produced in HYPOTHALAMUS but stored and released into bloodstream through pituitary

Releasing Hormone	Stimulated Hormone
Oxytocin	Stimulates milk production and uterine contractions. Involved in pair bonding, arousal. Secretion depends on electrical activity of neurons in the hypothalamus. During orgasm, body releases dopamine, known as "the feel-good hormone," and oxytocin, "the love drug." These hormones increase feelings of happiness and other positive emotions, and they counteract the "stress hormone," cortisol. Being mindful throughout your day can help reduce stress, increase oxytocin levels, and improve overall well-being.
Vasopressin (ADH or antidiuretic hormone)	Stimulates water reabsorption in kidneys, constricts arterioles. Inadequate production of vasopressin during sleep causes frequent urination.

Importance of Manganese on Pituitary Function

Manganese is required for normal thyroid function and is involved in the formation of thyroxin. Tissue mineral analysis (TMA) studies have revealed low manganese levels in hypothyroid patients. Due to the antagonistic effect of insulin, parathyroid hormone (PTH), and estrogen on thyroid function, absorption or utilization of manganese may be impaired when levels of these hormones are elevated.
The adrenal hormones are known to affect the tissue distribution of manganese as well as to alter its metabolism.

Reproductive function in manganese deficient patients is characterized by defective ovulation, ovarian and testicular degeneration, and increased infant mortality.

Mn-zyme

1.Watts DL: Indications of parathyroid activity in hair tissue mineral patterns. T.L.F.D., Oct. 1989.
2. Watts DL: The nutritional relationships of the thyroid. /. Orthomol. Med. 4,3, 1989.
3. Failla ML: Hormonal regulation of manganese. In: Manganese in Metabolism and Enzyme Function. Schrammk, V.L., Wedler, F.C., Eds. Academic Press, N.Y., 1986.

1. Orchestration and Regulation cont.

Pineal Gland

- Of the endocrine organs, the function of the pineal gland was the last discovered.
- Located deep in the center of the brain, the pineal gland was once known as the “third eye.”
- The pineal gland produces a single hormone - melatonin, which helps maintain circadian rhythm and regulate reproductive hormones.
  - Melatonin blocks the secretion of gonadotropins (luteinizing hormone and follicle stimulating hormone) from the anterior pituitary gland. These hormones aid in the proper development and functioning of the ovaries and testes.

Cytozyme B (neonatal Brain glandular) can directly affect pineal gland. Consider Melatonin (derived from serotonin) and supplementation with 5-HTP / Neuro-5-HTP Plus.

MIND-BODY CONNECTION

- **The pineal gland releases hormones such as melatonin, which helps regulate the body clock, but some people believe it may produce a psychedelic substance called DMT,** N,N-Dimethyltryptamine

- **In 2000, a clinical psychiatrist suggested in a book that the pineal gland produced enough DMT to produce psychoactive effects, but science has not confirmed this.**

- **'Mystical' Psychedelic Compound Found in Normal Brains** University of Michigan https://www.michiganmedicine.org/health-lab/mystical-psychedelic-compound-found-normal-brains

MIND-BODY CONNECTION

Mind–body research moves towards the mainstream European Molecular Biology Organization
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1456909/

Most scientists who became interested in this field said their efforts to investigate aspects of the mind–body connection were met with skepticism and even derision from the scientific mainstream. Esther Sternberg, a rheumatologist, a Senior Investigator in Neuroscience at the NIH, in 1980 studied the strange case of a man who developed severe scleroderma—an autoimmune disease—after taking an experimental epilepsy drug, which raised serotonin levels.

MIND-BODY CONNECTION

Candace Pert Molecules of Emotions - Neuropeptides

Correlation between Pineal Activation and Religious Meditation Observed by Functional Magnetic Resonance Imaging Nature Proceedings

https://www.nature.com/articles/npre.2007.1328.1

Psilocybin Research currently underway in many countries

PROTOCOL

- Spiritual, Religious practices, Prayer, meditation
- Sleep
- DAYLIGHT exposure
- Exercise
- Social circle, Relationships
- GlucoResolve or BioGlycozyme Forte
- Pituitary PT/HPT
- De-Stress
- Melatonin
- Alpha Theta Ultra PM
- Mn Zyme
- Bio C Plus
- Zn Zyme Forte

Foundations of Hormonal Balance

Address these questions first:

1. Diet
2. Digestion / Absorption / Elimination
3. Nutrient deficiencies
4. Parasites / candida / viruses
5. Toxins / heavy metals
6. Medications

Common Endocrine Disruptors

Common EDCs	Used In
DDT, Chlorpyrifos, Atrazine, 2, 4-D, Glyphosate	Pesticides
Lead, Phthalates, Cadmium	Children's Products
Polychlorinated biphenyls (PCBs) and Dioxins	Industrial Solvents or Lubricants and their Byproducts
Bisphenol A (BPA), Phthalates, Phenol	Plastics and Food Storage Materials
Brominated Flame Retardants, PCBs	Electronics and Building Materials
Phthalates, Parabeans, UV Filters	Personal Care Products, Medical Tubing, Suncreen
Triclosan	Anti-Bacterial Soaps, Colgate Total
Perfluorochemicals	Textiles, Clothing, Non-Stick Food Wrappers, Mircowave Popcorn Bags, Old Teflon Cookware