

Neuro-endocrine regulations of hormone action

MV

Mind and Body coupling

- **Interaction between the nervous system and the endocrine system.**
- **The nervous and endocrine systems often act together in a process called neuro-endocrine integration, to regulate various physiological processes.**
- **The neuroendocrine system is the mechanism by which the hypothalamus maintains homeostasis, regulating reproduction, metabolism, eating and drinking behaviour, energy utilization, osmolarity and blood pressure.**

- The neurons of the neuroendocrine system are large; they are mini *factories* for producing secretory products; their nerve terminals are large and organised in coherent terminal fields; their output can often be measured easily in the blood

Major neuroendocrine systems

- Hypothalamic–pituitary–adrenal axis (HPA axis)
- Hypothalamic–pituitary–thyroid axis (HPT axis)
- Hypothalamic–pituitary–gonadal axis (HPG axis)
- Hypothalamic–neurohypophyseal system

Monoamine neurotransmitters

- Histamine - a substance derived from the amino acid histidine that acts as a neurotransmitter mediating arousal and attention, as well as a pro-inflammatory signal released from mast cells in response to allergic reactions or tissue damage. Histamine is also an important stimulant of HCl secretion by the stomach through histamine H₂ receptors.
- Serotonin - a central nervous system neurotransmitter derived from the amino acid tryptophan involved in regulating mood, sleep, appetite, and sexuality.

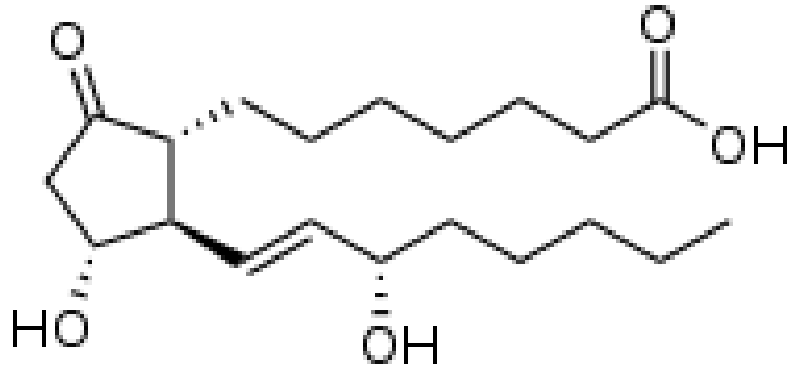
The three catecholamine neurotransmitters:

- Norepinephrine (nor-adrenaline) - a neurotransmitter involved in sleep and wakefulness, attention, and feeding behavior, as well as a stress hormone released by the adrenal glands that regulates the sympathetic nervous system.
- Epinephrine (adrenaline) - an adrenal stress hormone, as well as a neurotransmitter present at lower levels in the brain.
- Dopamine - a neurotransmitter involved in motivation, reward, addiction, behavioral reinforcement, and coordination of bodily movement

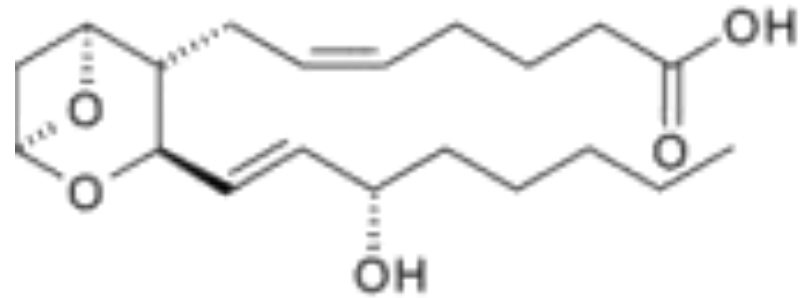
Eicosanoids

- The **eicosanoids** are considered "local hormones." They have specific effects on target cells close to their site of formation.
- Produced from arachidonic acid, a 20-carbon polyunsaturated fatty acid (5,8,11,14-eicosatetraenoic acid).

Chemical structure



Prostaglandin E₁. The 5-member ring is characteristic of the class.



Thromboxane A₂

Formed from Fatty Acid Sources

- "Eicosanoid" (*eicosa-*, Greek for "twenty") is the collective term for oxygenated derivatives of three different 20-carbon fatty acids:
 1. Eicosapentaenoic acid (**EPA**), an ω -3 fatty acid with 5 double bonds;
 2. Arachidonic acid (**AA**), an ω -6 fatty acid, with 4 double bonds;
 3. Dihomo-gamma-linolenic acid (**DGLA**), an ω -6 fatty acid, with 3 double bonds.

Major Eicosanoids

- Current usage limits the term eicosanoid to :
 1. Leukotrienes (**LT**)
 2. Eoxins (**EX**)
 3. three types of prostanoids :
 - prostaglandins (**PG**),
 - prostacyclins (a subset of **PG** termed **PGI**),
 - thromboxanes (**TX**).

Leukotrienes, eoxins and prostanoids are sometimes termed 'classic eicosanoids'

Eoxines

- Proinflammatory eicosanoids
- Produced by human eosinophils and mast cells

Leukotriene

- Isolated from leucocytes, derived from arachidonic acid
- Inflammatory mediators
- Autocrine and paracrine
- Trigger contractions in the smooth muscles lining the bronchioles
- Overproduction causes asthma and allergic rhinitis

Thromboxanes

- Produced by platelets
- Vasoconstriction
- Platelet aggregation
- Clot formation

Prostaglandins

- First isolated from seminal fluid in 1935
- Arachidonic acid derivative
- Vasodilators inhibit the aggregation of blood platelets
- Involved in inflammation
- Synthesized in the walls of blood vessels and serve the physiological function of preventing needless clot formation and contraction of smooth muscles

Chalones

- Endogenous growth-inhibiting factors
- Sir E. A. Shaefer (1913) chalone (Greek: to make slack)
- N-substituted oligopeptides found in extracts of Liver, Large intestine, melanocytes, lymphocytes and neuroblastoma
- All of them inhibit growth, even in tumor cells

- Bone marrow---PyroGlu-GluAspCys-Lys
- 3-7 aa
- Non-toxic, reversible action with tissue preference

Phytohormones

- Phytohormones are chemical messengers that coordinate cellular activities in plants. Common among plant hormones are auxins, cytokinins, gibberellic acid, brassinosteroids, ethylene, abscisic acid, salicylic acid and jasmonic acid.
- Any of various hormones produced by plants that control or regulate germination, growth, metabolism, or other physiological activities.

Synthetic hormones

- Synthetic chemical compounds which mimic the activity of endogenous hormones produced in the body, but which differ in structure from naturally occurring hormones.

Uses

- Synthetic estrogens [most notably ethinylestradiol, in combination with synthetic progestins, are used in contraceptive and hormone replacement therapy formulations.
- Synthetic glucocorticoids are prescribed widely as anti-inflammatory agents. Antiestrogens, aromatase inhibitors, and antiandrogens are prescribed for cancer therapy.
- Diethylstilbestrol is a synthetic non-steroidal estrogen that was first synthesized in 1938 and then prescribed to several million women between 1940 and 1971 to prevent threatened miscarriage in the first trimester, before untoward side effects stopped this practice.
- All these compounds may be released into the environment not only as the parent compound, but also as the metabolites in the urine and feces of people who use them as medications.