Physiology of Hypothalamus and Pituitary

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Pituitary Gland

- Pituitary gland (hypophysis) is two different tissue types that merged during embryonic development
  - *Anterior pituitary* (adenohypophysis): true endocrine gland of epithelial origin
  - *Posterior pituitary* (neurohypophysis): extension of the neural tissue of the brain
    - secretes neurohormones made in the hypothalamus

Pituitary Gland

- Pituitary bridges and integrates the neural and endocrine mechanisms of homeostasis.

- Highly vascular
  - Posterior pituitary receives arterial blood
  - anterior pituitary receives only portal venous inflow from the median eminence.

- Portal system is particularly important in its function of carrying neuropeptides from the hypothalamus and pituitary stalk to the anterior pituitary.

Posterior Pituitary

- Storage and release site for two neurohormones (peptide hormones)
  - Oxytocin
  - Vasopressin (antidiuretic hormone; ADH)

- Large diameter neurons producing hormones are clustered in hypothalamus at paraventricular (oxytocin) and supraoptic nuclei (ADH)
- Secretory vesicles containing neurohormones transported to posterior pituitary through axons of the neurons
- Stored at the axons until a release signal arrives
- Depolarization of the axon terminal opens voltage gated Ca2+ channels and exocytosis is triggered
- Hormones release to the circulation

Posterior Pituitary

- The posterior pituitary regulates water balance
  and uterine contraction

  - Vasopressin (ADH), is a neuropeptide hormone that acts on the collecting duct of the kidney to increase water reabsorption

  - Oxytocin principal biological action is stimulation of smooth muscle contraction by the uterus during parturition and by the mammary gland during suckling

Antidiuretic Hormone (ADH-vasopressin)

- Decreased excreation of water by the kidneys (antidiuresis)

- Permeability of the collecting ducts and tubules to water increases and allows most of the water to be reabsorbed,thereby conserving water in the body and producing very concentrated urine

- Insertion of aquaporins to the luminal membranes of the tubular epithelial cells
  - ADH receptors activate adenylyl cyclase
  - Formation of cAMP
  - Phosphorylation of in vesicles containing aquaporins
  - Insertion of aquaporins to the mebrane

Antidiuretic Hormone (ADH-vasopressin)

- Stimulation of ADH secretion
  - Increased extracellular fluid osmolarity
    - Osmoreceptors in or near the hypothalamus
    - Stimulation of supraoptic nuclei
  - Low blood volume and low blood pressure
    - Blood volume decrease by 15-25% or more
    - Decreased strech of the baroreceptors of the carotid, aortic and pulmonary regions stimulate
    - Secretion of ADH rises to as high as 50 times normal
    - High concentrations of ADH constricts arteriols and increase arterial pressure

Oxytocin

- Stimulates contraction of the pregnant uterus, especially toward the end of gestation
  - In a hypophysectomized animal, the duration of labor is prolonged
  - amount of oxytocin in the plasma increases during labor, especially during the last stage
  - stimulation of the cervix in a pregnant animal elicits nervous signals that pass to the hypothalamus and cause increased secretion of oxytocin.

- Milk ejection by the breasts
  - In lactation, oxytocin causes milk to be expressed from the alveoli into the ducts of the breast

  - Suckling stimulus on the nipple of the breast causes signals to be transmitted through sensory nerves to the oxytocin neurons in the paraventricular and supraoptic
  - release of oxytocin by the posterior pituitary gland
  - oxytocin is carried by the blood to the breasts, where it causes contraction of myoepithelial cells

Anterior Pituitary

- Major endocrine gland
- Hormone secretion is controlled by hypothalamus
- Secretes six hormones
  - prolactin (PRL)
  - thyrotropin (TSH)
  - adrenocorticotropin (ACTH)
  - growth hormone (GH-somatotropin)
  - follicle-stimulating hormone (FSH)
  - luteinizing hormone (LH)

Portal System

- A portal system connects the hypothalamus and anterior pituitary
- Portal system: special modification of the circulatory system two sets of capillaries connected in series by a set of small veins
  - Neurohormones enter the system at the first set of capillaries and go directly through the portal vein to the second capillary bed and diffuse out
  - Small amount of hormone (neurosecretory cells) is sufficient

Hypothalamus & Anterior Pituitary

- *Releasing hormones:* hypothalamic neurohormones that control release of anterior pituitary hormones (e.g., thyrotropin-releasing hormone)

- *Inhibiting hormones:* hypothalamic neurohormones that control inhibition of release of anterior pituitary hormones (e.g., growth hormone-inhibiting hormone)

- *Trophic hormones:* control the secretion of other hormones (all ant. pit. hormones except prolactin)
  - -tropin (e.g., gonadotropin)

Anterior Pituitary

- Anterior pituitary hormones control growth, metabolism, and reproduction
- Growth hormone affects metabolism of many tissues in addition to stimulating hormone production by the liver
- Prolactin (PIH) and growth hormone (GHIH-somatostatin)are the only two anterior pituitary hormones with hypothalamic release inhibiting hormones
- Other than prolactin and growth hormone, all four hormones have another endocrine gland as their primary target.

Growth Hormone (somatotropin)

- Released throughout life
  - biggest role in children
  - peaks during teenage years
  - anabolic

Growth Hormone

- Regulation in hypothalamus
  - growth hormone-releasing hormone (GHRH)
  - growth hormone-inhibiting hormone (somatostatin-SS)

- On a daily basis, pulses of GHRH from the hypothalamus stimulate GH release
  - In adults, the largest pulse of GH release occurs in the first two hours of sleep

Growth Hormone

- Feedback Control
  - Two hypothalamic hormones (GHRH and somatostatin)
  - Two systemic signals (GH and IGFs)

Growth Hormone

- Plasma-growth hormone binding protein
  - protects plasma GH from being filtered into the urine
  - extends half-life
- Target tissues are both endocrine and nonendocrine cells
- Acts as a trophic hormone to stimulate secretion of insulin-like growth factors (IGFs)

Growth Hormone

1. GH and IGFs promote protein synthesis (especially in skeletal muscle)
    1. Enhancement of amino acid transport through the cell membranes
    2. Enhancement of RNA translation to cause protein synthesis by the ribosomes
    3. Increased nuclear transcription of DNA to form RNA
    4. Decreased catabolism of protein and amino acids

2. GH enhances fat utilization for energy

3. GH decreases carbonhydrate utilization
    1. causes lipolysis, decreased glucose uptake by muscle, and gluconeogenesis in the liver (increase blood glucose concentrations)
    2. Increased insulin secretion (*diabetogenic*)

4. Insulin and Carbonhydrate are necessary for growth-promoting action of growth hormone

5. Both GH and IGFs act on bones to increase bone growth (only IGFs stimulate cartilage synthesis directly)

Growth

- Two types of growth
  1. Soft tissue growth
  2. Linear bone growth

- Multiple hormones have direct or permissive effects
- Involvement of paracrine factors

Bone growth

- GH increases growth of the skeletal frame
  - Increased deposition of protein by the chondrocytic and osteogenic cells that cause bone growth
  - İncreased rate of reproduction of the cells
  - Specific effect of converting chondrocytes into osteogenic cells, thus causing deposition of new bone

Bone Growth

- Growth hormone stimulation
  - Long bones grow in length at the epiphyseal cartilages (lengthening)
    - Deposition of new cartilage and conversion into new bone
    - Ends by late adolescence
  - Osteoblasts in the bone periosteum and in some bone cavities deposit new bone on the surfaces of older bone (thickening)
    - Especially membranous bones (e.g., jaw bones)

Bone Growth

- Somatomedins
  - Synthesized in liver by growth hormone stimulation
  - Has longer half-life than growth hormone
  - Effects on growth are similar to insulin (so called IGFs)
  - growth effects of growth hormone result from somatomedin C and other somatomedins, rather than from direct effects of growth hormone on the bones and other peripheral tissues

  - Deficiency of Somatomedin C (IGF-1) synthesis → dwarfism

Soft Tissue Growth

- Growth hormone
- Thyroid hormone
- Insulin

- Growth hormone and IGFs → tissue protein synthesis and cell division
  Hypertrophy (increased cell size)
  Hyperplasia (increased cell number)
- Thyroid hormone → permissive role in growth
  → contribute directly to nervous system development
  Children with untreated hypothyroidism (cretinism) do not grow to normal height even if they secrete normal amounts of growth hormone

- Insulin → stimulation of protein synthesis and provides energy in the form of glucose
  → permissive for growth hormone
  insulin-deficient children fail to grow normally even though they may have normal concentrations of growth and thyroid hormones

Growth Hormone Deficiencies

- Essential for normal growth
- Dwarfism:
  - Severe growth hormone deficiency in childhood
  - Problem with growth hormone synthesis or with defective GH receptors

- Acromegaly:
  - Adults with excessive secretion of growth hormone
  - Cartilage, soft tissue growth, thickening of the membranous bones
  - Lengthening of the jaw, coarsening of facial features, and growth of hands and feet

- Giantism:
  - Oversecretion of growth hormone in children (+ linear bone growth)