**Hypothalamus and Pituitary Gland**

--both are master endocrine glands (since they control other glands)

**Hypothalamus**

--receives input from cortex, thalamus, limbic system, and internal organs
--controls pituitary gland with releasing and inhibiting hormones
--hormones are only around pituitary, not in general circulation
--Supraoptic and paraventricular nuclei regulate secretory activity of pituitary gland via neurohormones (releasing and inhibiting hormones) and APs

**Pituitary Gland (hypophysis)**

--secretes 9 major hormones and stimulating hormones
--Anterior Lobe: 75%, develops from roof of mouth (Rathke’s pouch)
  * adenohypophysis
  * consists of three areas: pars distalis, pars intermedia, pars tuberalis
--Posterior Lobe: 25%, end of axons of 10,000 neurons found in hypothalamus, neuroglial cells called pituicytes
  * neurohypophysis
  * continuous with the brain
  * secretes neurohormones that enter capillaries and the systemic circulation
  * does not synthesis hormones

**Anterior Pituitary Gland Hormones**

1. Growth Hormone (hGH)/Somatotropin
   * Produced by: somatotrophs
   * Target Cells: liver, skeletal muscle, cartilage, and bone
   * Actions
     a. INCREASES synthesis of insulinlike growth factors (IGFs) = SOMATOMEDINS that act locally or enter bloodstream
     b. increase growth via hypertrophy and hyperplasia by increasing their uptake of amion acids and synthesis of proteins
     c. Stimulate lipolysis in adipocytes so fatty acids are used for ATP
     d. Stimulate glycogenolysis and gluconeogenesis in liver (increase blood glucose level)
     e. retard uptake of glucose by muscle so blood glucose levels remain high enough to supply brain
   **Blood glucose levels up, AA levels down**
   *Regulation of hGH
     a. Low blood sugar stimulates release of GHRH from hypothalamus → ant. pituitary releases more hGH → more glycogen broken down into glucose by liver cells

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   *Regulation of hGH
     a. Low blood sugar stimulates release of GHRH from hypothalamus → ant. pituitary releases more hGH → more glycogen broken down into glucose by liver cells
b. High blood sugar stimulates release of GHIH from hypothalamus \(\rightarrow\) less hGH from ant. pituitary \(\rightarrow\) glycogen does not breakdown into glucose

*Diabetogenic/anti-insulin Effect of hGH
a. Excess of growth hormone may lead to insulin resistance and glucose intolerance (raises blood glucose conc., pancreas releases insulin continually, beta-cell burnout)
b. Diabetogenic effect: eventually causes diabetes mellitus if no insulin activity can occur

*Disorders of hGH
a. Acromegaly: increase GH after puberty (bones grow in width, thickening of bones)
b. Gigantism: too much GH before puberty
c. Dwarfism: lack of GH before puberty

*Factors Affecting Growth Hormone Secretion

<table>
<thead>
<tr>
<th>Stimulatory Factors</th>
<th>Inhibitory Factors</th>
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<tbody>
<tr>
<td>Decrease glucose concentration</td>
<td>Increased glucose concentration</td>
</tr>
<tr>
<td>Decreased free fatty acid concentration</td>
<td>Increased free fatty acid concentration</td>
</tr>
<tr>
<td>Arginine</td>
<td>Obesity</td>
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<tr>
<td>Fasting or starvation</td>
<td>Senescence</td>
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<tr>
<td>Hormones of puberty (estrogen/ testostereone)</td>
<td>Somatostatin</td>
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<tr>
<td>Exercise</td>
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<tr>
<td>Stress</td>
<td>Growth hormone</td>
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<tr>
<td>Stage III and IV sleep</td>
<td>Beta-adrenergic agonists</td>
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<tr>
<td>Alpha-adrenergic agonists</td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>

2. Thyroid Stimulating Hormone (TSH)
*Glycoprotein with alpha and beta subunits
*Regulated by: hypothalamus
*Secreted by: thyrotroph cells
*Actions:
  a. stimulates the synthesis and secretion of T3 (triiodothyronine) and T4 (thyroxine)
b. Metabolic rate stimulated
*Secretion: diurnal
*Disorders of TSH
a. Hypothyroidism/cretinism: deficiency of TSH in childhood
b. Hypothyroidism/myxedema: deficiency of TSH in adulthood
c. Hyperthyroidism/thyrotoxicosis/Graves’ disease: excess TSH
3. Follicle Stimulated Hormone (FSH)
   *Regulated by: Gonadotropin Releasing hormone (GnRH) from the hypothalamus
   *Released by: gonadotroph cells

   *Actions in Females
   - a. initiates the formation of follicles within the ovary
   - b. stimulates follicle cells to secrete estrogen

   *Actions in Males
   - a. stimulates sperm production in testes

   *Disorders of FSH
   - a. Hypogonadism: failure of germ cell maturation, deficiency of FSH

4. Luteinizing Hormone (LH)
   *Regulated by: HnRH from hypothalamus
   *Released from: gonadotroph cells
   *Action in Females
   - a. LH stimulates ovary to secrete estrogen, ovulation of secondary oocyte, formation of corpus luteum (which secretes progesterone)

   *Action in Males
   - a. stimulates interstitial/Leydig cells to secrete testosterone

   *Disorders of LH
   - a. Hypogonadism: failure of sexual maturation, deficiency of LH

5. Prolactin (PRL)
   *Regulated by: hypothalamus
   - a. suckling reduces levels of hypothalamic inhibition and prolactin levels rise along with milk production
   - b. nursing ceases and milk production slows

   *Secreted by: lactotrophs
   *Actions
   - a. causes milk production/synthesis
   - b. stimulates breast development, lactogenesis
   - c. inhibits ovulation
   - d. increased release during night/sleep (10pm-7am)

6. Adrenocorticotrophic Hormone (ACTH)/Corticotropin
   *Regulated by: corticotrophic releasing hormone (CRH) from hypothalamus
   *Released from: corticotrophs
   *Actions:
   - a. stimulates cells of the adrenal cortex

   *Disorders of ACTH
a. Addison’s Disease: deficiency of ACTH
b. Cushing’s Disease: excess of ACTH

7. Melanocyte-Stimulating Hormone
   *Regulated by: CRH from hypothalamus
   *Released from: corticotrophs from pars intermedia
   *Actions:
     a. function not certain in humans (increased skin pigmentation in frogs)

Posterior Pituitary Hormones

1. Antidiuretic hormone (ADH)/vasopressin/arginine vasopressin
   *Synthesized in: supraoptic nucleus
   *Actions:
     a. decrease water loss to decrease blood osmolality → decrease urine production by increasing water reabsorption from kidneys, decrease sweating
     b. increase blood pressure
   *Regulation
     a. major stimulus: increased plasma osmolarity
     b. dehydration: ADH released
     c. Overhydration: ADH inhibited
   *Disorders of ADH
     a. Diabetes Insipidus: lack of ADH, excessive H2O loss, dehydration
     b. Syndrome of inappropriate ADH secretion: excess ADH, hypertension

2. Oxytocin
   *Synthesized in: paraventricular nucleus
   *Target tissues: uterus and mammary glands
   *Actions:
     a. During delivery: baby’s head stretches cervix, hormone release enhances uterine muscle contraction (prostaglandins), baby and placenta delivered
     b. After delivery: suckling and hearing baby’s cry stimulates milk ejection, hormone causes muscle contraction of lactiferous ducts and milk ejection ‘milk letdown’
Pineal Gland/Epiphysis

Characteristics

--small gland attached to roof of 3rd ventricle of brain (diencephalon)
   *no direct nerve pathway b/w CNS and epiphysis
--Consists of pinealocytes and neuroglia
--Sympathetic innervation of the pineal gland from superior cervical ganglion
--Cells look like cone cells of retina, “third eye”
--Detects sensitivity of light

Hormones

1. Melatonin
   *serotonin is its synthetic precursor
   *Secreted: in the dark periods of the day
      a. melatonin secretion producing sleepiness occurs during darkness
         due to lack of stimulation from sympathetic ganglion, nocturnal
         melatonin release spikes decrease with age
   *Regulation:
      a. sympathetics: inhibits release of melatonin
      b. posterior hypothalamus detects enzyme state: hypocretin (orexin)
         stimulates appetite, arousal, lack leads to narcolepsy
   *Action:
      a. enhance sleep (circadian rhythm)
      b. can decrease GnRH from hypothalamus inhibiting reproductive
         functions
c. induces natural sleep (w/o side effects of sedatives)
d. inhibits reproductive hormones (onset of puberty may be due to a
decrease in melatonin)
e. may be useful as a contraceptive
f. antioxidant (may slow aging process)
g. enhances immunity

*Disorders of Melatonin
a. Seasonal Affective Disorder (SAD): depression w/i winter moths
due to overproduction of melatonin (therapy: exposure to several
hours of light/day)
b. Jet Lag: helps to speed recovery

2. Arginine Vasotocin
   *AA derivative
   *Actions:
   a. regulates function of reproductive system in some animals

Parathyroid Gland

Characteristics
--found on back of thyroid gland
--Cell types
   a. Principal/Chief Cell: produces parathyroid hormone (PTH)
   b. oxyphil cell: function unknown

Parathyroid Hormone
--Target Organs:
   a. kidneys
      *slows rate of calcium and magnesium loss from blood into the curine
      (stimulates resoprtion of Ca and Mg)
      *increases loss of $\text{HPO}_4^{2-}$ from blood into urine for a net decrease of
      $\text{HPO}_4^{2-}$ in plasma (more loss than gain from bone)
      *stimulates formation of calcitriol (active form of vit. D)
   b. GI
      *indirectly: calcitriol increases intestinal absorption of Ca, Mg, $\text{HPO}_4$
   c. bone
      *stimulates osteoclasts resulting in bone resorption and increase of
calcium and $\text{HPO}_4^{2-}$ in blood

--Regulation
*High or low blood levels of calcium stimulate the release of different hormones (PTH or CT)*

*Negative feedback is directly on secretion of hormones, no involvement of pituitary*

--Actions:

a. Raises blood calcium levels:
   - Increases activity of osteoclasts
   - Increases reabsorption of calcium by kidney
   - Inhibits reabsorption of phosphate
   - Promotes formation of calcitriol (vitamin D₃) by kidney which increases absorption of calcium and magnesium by intestinal tract

b. Opposite function of calcitonin

--Disorders of Parathyroid Gland

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<thead>
<tr>
<th></th>
<th>Hypoparathyroidism</th>
<th>Hyperparathyroidism</th>
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<tbody>
<tr>
<td>Causes</td>
<td>Accidental removal during thyroidectomy</td>
<td>Primary hyper: result of abnormal function (tumors)</td>
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<td></td>
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<td>Secondary hyper: caused by conditions that reduce blood Ca levels</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Hypocalcemia, normal bone structure, increased neuromuscular excitability, flaccid heart muscle</td>
<td>Hypercalcemia, bones weaken, neuromuscular system less excitable, increased force of contraction of cardiac muscle</td>
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