**Syllabus:**

**Lecture 1: Introduction to Neuroendocrinology: Hypothalamus and Pituitary**
- Anatomy of the hypothalamus, pituitary and median eminence
- Hypophysiotrophic hormones
  - TRH, CRH, GnRH, GHRH, Somatostatin, Dopamine, PACAP
  - Melanocortins
- Posterior Pituitary
  - Oxytocin, Vasopressin
- Feedback loops
  - Negative feedback (engineering analogy)
  - Positive feedback (oxytocin)
- Homeostatic Feedback
  - 3-tiered (basic since these will be covered later in class; HPT, HPA, HPG)
  - 2-tiered (more detail here; Prolactin, GH)
- Reflexive Feedback
  - Fixed: oxytocin
  - Graded: Vasopressin
- Characteristics of blood brain barrier (paper by Muller et al; 2010 illustrating structural differences at the level of the median eminence and third ventricle)
- Diseases of Pituitary regulation

**Lecture 2: Hypothalamic Pituitary Thyroid (HPT) Axis**
- Thyroid gland
  - Gross anatomy
  - Follicle cell
- Thyroid hormone (TH): synthesis, release, metabolism (deiodonase)
  - TH receptors: genomic and non-genomic signaling
  - TH cellular and systemic effects
- Thyrotropin releasing hormone (TRH): location, secretion, metabolism, receptor
- Thyroid stimulating hormone (TSH): structure, receptor, cellular effects
- Somatostatin
- Negative feedback: Ultrashort, short, long
- TRH like peptides
- Neural regulation of negative feedback to TRH
  - Brainstem catecholamine neurons (cold)
  - Hypothalamic arcuate nucleus
Hypothalamic dorsomedial nucleus
Effects of fasting and leptin on HPT axis

**Lecture 3: Hypothalamic Pituitary Adrenal (HPA axis)**

Introduction
- Adrenal Gland
- Stress Response
- Stress neurocircuitry

Adrenal hormones
- Mineralocorticoids, Aldosterone
- Glucocorticoids
  - Systemic action
  - Receptors

Corticotropin Releasing Hormone (CRH)
- Brain CRH system, receptors
- Urocortins
- CRH binding protein

Adrenocorticotropic hormone (ACTH): derivation from Pro-opiomelanocortin gene, receptor, signaling

Feedback
- Glucocorticoids
- Vasopressin

Afferent neural regulation of the PVN CRH neurons

Adrenalectomy

Chronic Stress
- Desensitization and habituation
- Metabolic syndrome

**Lecture 4: Hypothalamic Pituitary Gonadal (HPG) axis**

Male
- HPG axis
- Testosterone effects
  - Signal transduction: Lutenizing hormone (LH), Follicle stimulating hormone (FSH), testosterone
  - Common features: male and female HPG
  - Why males do not cycle

Female
- Reproductive cycle definition
- Female HPG axis
- Menstrual cycle: tissue events
- Menstrual cycle: hormonal events
- Estrogen effects, receptor signaling

Reproductive centers of the brain
- Hypothalamus: anterior/preoptic area, ventrobasal input, nucleus sagitalis
- Sexual dimorphism (male/female; homosexual male)
Mechanisms underlying the LH surge

How the gonadotrope selectively controls FSH vs LH secretion

- Inhibin, activin, follistatin
- GnRH pulses
- PACAP
- Gonadotropin inhibitory hormone

Shift in estrogen from negative to positive feedback during the LH surge

- GnRH pulsatility, receptor signaling
- Sex hormone feedback to GnRH
- Astrocytic progesterone
- Interaction between estrogen and neuroprogesterone
- Arcuate kisspeptin neurons
- Differential feedback model

Energy homeostasis

- Kisspeptin neurons and leptin
- Orexins
- Steroidogenic factor-1 (SF-1)

**Lecture 5: The neuroendocrine regulation of energy balance**

Historical lesioning studies

Neuroanatomy

Hypothalamic regulation of the sympathetic nervous system

- Glucose homeostasis (liver, pancreas)
- Hypoglycemia and counterregulation
- Free fatty acids

Regulation of energy balance

Neuropeptides

- Arcuate nucleus (neuropeptide Y, melanocortins)
- Lateral hypothalamus (orexin, melanin concentrating hormone)
- Ventromedial nucleus (brain derived neurotrophic factor, PACAP, SF-1)
- Paraventricular nucleus (CRH, TRH, oxytocin, galanin)

Feedback signals

- Satiety hormones (insulin, leptin)
- Nutrient signals (glucose, fatty acids, amino acids)
  - Glucose and fatty acid sensing neurons
  - Integration of nutrient signals
- Nutrient related signals (gut peptides)
  - Satiety (cholecystokinin, glucagon-like peptide, peptide YY, apolipoprotein, enterostatin, bombesin-family, amylin)
  - Orexogenic: ghrelin

Feedback loops

Reward pathway
Fasting and obesity/Diabetes

Lecture 6: Neuroendocrine regulation of biological rhythms

Biological rhythms defined
- Ultradian, circadian (focus), infradian
- Circadian rhythm of metabolic enzymes as examples

Pacemakers
- Suprachiasmatic nucleus (SCN)
- Clock genes
- Mechanisms of light entrainment

Melatonin and pineal gland
- SCN regulation of the pineal (sympathetic innervations)
- Melatonin receptors and physiological functions
- Seasonal effects

Metabolic regulation of clock genes

Other entrainers (meal pattern, activity, body temperature)

Glucocorticoids stabilize the SCN

Circadian disruption
- Jet lag
- Metabolic disease
- Cancer

Lecture 7: Neuroendocrine Immunology

Overview of the immune system

Functions of the immune system:
1. Attack foreign organism or diseased cells
2. Provide energy for these tasks

Immune system and the brain

Interactions between the immune system and other neuroendocrine systems

Relationship between the immune system and energy balance

“How the immune systems uses the neuroendocrine system to feed it”

Circadian regulation of the immune system

Illness induced anorexia-cachexia vs starvation

Metabolic disease and inflammation