PHPY 5085Q – Neuroendocrinology: Regulation of Physiological Processes
Spring 2016: TBA
Tuesdays & Thursdays, 4:30 PM to 6:30 PM

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