Chapter 11

- Brain Mechanisms: Evidence
    - Hunger and satiety (feeling full) signals arise from the periphery and reach the brain.
    - Eating and drinking are evolutionary ancient (i.e. involve the brain stem)
    - Control mechanisms do not require the cortex. Decerebrated animals
        - Cannot seek food (cognitive behavior, they cannot just go get food, you have to feed them – seeking food/water is involved in the cortex)
        - Can eat, can respond to hunger and thirst
        - Can differentiate different kinds of food
        - Can vomit/reject bad food: area *postrema* is intact
- Hypothalamus
    - Lateral hypothalamus
        - Control hunger
        - Lesion → decrease eating/drinking and body weight
        - Stimulation → increase eating/drinking
        - Block glutamate transmission → decrease food intake
        - Doesn't just work by itself, it needs inputs to help it
            - LH need inputs → hunger and food intake are active processes
        - 2 types of neurons producing:
            - Melanin Concentrating Hormone (MCH)

- Orexin (a.k.a. hypocretin)

- Food deprivation increases MCH, Satiety decreases MCH
- Stimulation of MCH/orexin neurons: appetite inducing, decrease metabolic rate, increase motivation and movement
- MCH/orexin neuros project to areas involved in planning, motivation and movement
- MCH = a 'hunger' variable?
- What triggers the Lateral Hypothalamus MCH and Orexin neurons?
    - NeuroPeptide Y (NPY)
    - NPY injections in Hypothalamus: eating frenzies. Rats will tolerate pain in order to eat → NPY increases motivation to eat
    - NPY from the Arcuate nucleus (in hypothalamus, near 3rd ventricle)
    - NPY secretion is triggered by brain stem nuclei and controlled by stomach secretions (Ghrelin)
    - Endocannabinoids act like NPY. Marijuana used to increase appetite in chemotherapy patients.
    - Summary:
        - Stomach (Ghrelin) or Brain Stem (Liver) → Arcuate (NPY) → Lateral Hypothalamus (MCH & Orexin) → increase eating and decrease metabolism
- How do we stop eating? Two parallel inhibitory pathways
    - Leptin (from fat cells) inhibits the NPY neurons in the Arcuate Nucleus

- Cocaine and Amphetamine Regulated Transcript (CART) neurons in the Arcuate Nucleus. CART (and alpha-MSH) neurons inhibit the MCH/Orexin neurons via the MC-4R receptor
    - Satiety:
        - Leptin → -NPY and +CART → (+NPY or -CART) MCH/Orexin

- Leptin
    - hereditary leptin deficiency (OB-like) in humans. Genetic deficit in the production of Leptin.
    - Leptin no longer used in weight loss diets: Leptin resistance.
- Ingestive Behaviors: Obesity
    - Increasing problem: obesity → diabetes
        - Type 1 diabetes: deficiency in insulin production (requires injections)
        - Type 2 diabetes: deficiency in insulin receptors (treated with pills)
    - Average energy consumption: muscles 20%, brain 20 %, temperature regulation/heat & digestion 60%
        - Body weight is related to the energy that is stored or energy that is spent
    - Definition of obesity: more than 20% of normal weight
    - Body Mass Index (BMI): body fat based on height and weight
        - 25-30 = overweight
        - 30-40 = obese
        - 40+ = morbidly obese
    - why are people overweight?
        - On average: 2,500 kCal in, but only 300 kCal out…

        - Kind of foods eaten: high fat, high sugar, high calories
        - Not enough activity (we do only about 1/3 of what would be required)
        - Overwriting of physiological signals for satiety: encouraged to eat more, large portions.
        - Availability of (bad) foods.
    - Biological Causes:
        - Metabolic disorder (more calories in than out). Due to fast metabolism. In general, not due to a deficiency in Leptin production
        - High metabolic rates → increase availability of calories → spent if needed, stored if not (hence, obesity)
            - Low metabolic rates → no opportunity for fat storage
        - Genetic factors: different metabolic rates.
            - Twin studies (tested with high/low calorie diets)
            - Epidemiological studies (study of populations)
                - E.g. Pima Indians in the US vs. Mexico
    - Mouse: obesity is due to leptin deficit
    - Human: no evidence for leptin production deficits, but: Deficit in leptin transport through the blood-brain barrier. Deficit in sensitivity of leptin receptors (MC4 Receptors, age related)
    - In humans, high fat diets inherently decrease satiety signals.
    - Night Eating Syndrome (NES): more Ghrelin and less leptin at night.
    - ~25% of obese people have it in their genes. (very little that can be done to help them with their weight because the weight comes back)

- Treatment
    - Exercise (especially young age)
    - Wire in Jaw (close the mouth) and liquid diet
    - Gastroplasty: Reshaping the stomach
    - Intestinal bypass (directly to the large intestine)
    - Gastric bypass: 35% success in long-term decrease in weight. Diminish secretion of Ghrelin. (living without a stomach)
    - Gastric bubble. (swallow a bubble and decrease area in stomach to help you feel full quicker)
    - 5-HT promoters (relapse, cardiovascular side effects)
    - Uncoupling protein (UCP). Convert nutrient to heat.
- Conclusions:
    - Eat slowly
    - Eat regularly
    - Exercise (but not too much)
    - Don't eat at night

- Ingestive Behaviors: Anorexia Nervosa
    - Definition:
        - Refusal to maintain weight over the lowest weight considered normal for age/height
        - Intense fear of gaining weight or becoming fat (even when underweight).
        - In women: three consecutive missed menstrual periods, without pregnancy.
    - Can be explained by genes, society and social pressure.
    - Most deadly psychiatric disease, more than depression.

- 80% of cases are young women (age:15-24). 15% death rate.
- Can be due to too much exercise. (too much exercise decrease hunger signals). Restricting food results in increase physical activity (and weight loss).
- Respond physiologically correctly to food → not a loss of interest in foods.
- In normal, >6 months starvation has psychological consequences. OCD?
- Genetic factors (evidence by twin studies)
- Brain imbalance of NE, 5-HT and NPY. No effective drug treatment.
- Treatment: Psychotherapy.