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 neurons 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 3\textsuperscript{rd} 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.