**Brain mechanisms: evidence**

- Hunger and satiety signals arise from the periphery and reach the brain.
- Eating and drinking and drinking are evolutionarily ancient (i.e., involve the brain stem).
- Control mechanisms do not require the cortex.

  - **Decerebrate animals**
    - Cannot seek food
    - Can eat/drink, can respond to hunger and thirst
    - Can differentiate different kinds of food
    - Can vomit, reject bad food \(-\) area postrema is intact

**Hypothalamus**

- **Lateral hypothalamus (LH)**
  - Control hunger
  - Lesion \(-\) decrease eating/drinking and body weight
  - Stimulation \(-\) increase eating/drinking
  - Block glutamate transmission to LH \(-\) decrease food intake
    - LH needs inputs \(-\) hunger and food intake are active processes

**Hypothalamus and hunger**

- **Lateral hypothalamus (LH) and hunger**
  - 2 types of neurons producing:
    - Melanin concentrating hormone (MCH)
    - Orexin (recall... sleep chapter)
  - Food deprivation increases MCH in LH satiety decreases MCH
  - Stimulation of MCH Orexin neurons \(-\) appetite inducing, decreasing metabolic rate, increasing motivation and movement
  - MCH/orexin neurons project to areas involved in planning, motivation, and movement
    - MCH= a cephalic hunger variable?
  - What triggers the LH MCH and orexin neurons?
    - Neuropeptide Y (NPY)
      - NPY injections in hypothalamus: eating frenzies. Rats will tolerate pain in order to eat \(\rightarrow\) NPY increases motivation to eat
      - NPY secreted 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
- LH/ hunger summary

Hypothalamus and satiety
- 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 α-MSH) neurons inhibit the MCH/Orexin neurons via the MC-4 receptor
- Satiety

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

Figure 23 Hereditary Leptin Deficiency. The photographs show three patients with hereditary leptin deficiency before (a) and after (b) treatment with leptin for eighteen months. The faces of the patients are obscured for privacy. Two normal weight nurses are shown for comparison purposes.
**Ingestive behaviors: obesity**

- An increasing problem: obesity -> diabetes
- Type 1 diabetes: deficiency in insulin production (requires injections)
- Type 2 diabetes: deficiency in insulin receptors (treated with pills)
  - Correlation between obesity and diabetes
- Average energy consumption:
  - 20% muscles
  - 20% brain
  - 60% heat regulation and digestion
  - Body weight <=> energy stored - energy spent
- Definition of obesity: more than 20% above normal weight
- Body mass index (BMI): body fat based on height and weight
  - 25-30: overweight
  - 30-40: obese
  - 40 and above: morbidly obese
- Why are people overweight
  - On average: 2,500 kCal in, but only 300 kCal out
  - Kind of food eaten: high fat, high sugar, high calories
  - Not enough activity (⅓ of what would be required)
  - Encouraged to eat more -> overwriting of physiological signals for satiety
  - Availability of bad foods
- Mouse: obesity is due to leptin deficit
- Human: no evidence for leptin production deficits in obese patients but:
  - Deficit in leptin transport through the BBB
  - Deficit in sensitivity of leptin receptors (MC-4 receptors, age related)
- In humans, high fat diets inherently decrease satiety signals -> obesity
- Night eating syndrome (NES): more Ghrelin and less leptin at night
- Treatments:
  - 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
  - Gastric bubble
  - 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
Obesity

- Biological causes of obesity:
  - Metabolic disorder (more calories in than out). Due to fast metabolism
    - In general, not due to a deficiency in leptin production
  - 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
  - High metabolic rates -> increase availability of calories -> spent if needed, stored if not (hence, obesity)
  - Low metabolic rates -> no opportunity for fat storage (hence, no obesity)

Ingestive behaviors: anorexia nervosa

- Definition
  - Refusal to maintain weight over the lowest 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
- 80% of cases are young women (age: 15-24).
  - 15% death rate
- Can be due to too much exercise (too much exercise decreases hunger signals). Restricting food results in increase physical activity (and weight loss)
- Respond physiologically correctly to food -> not a loss of interest in foods
- Genetic factors (evidenced by twin studies)
- Brain imbalance of NE, %-HT and NPY. no effective drug treatment
- Treatment: psychotherapy