Brain mechanisms: Evidence

- Hunger and satiety signals arise from periphery and reach the brain.
- Eating and drinking are evolutionarily ancient (brain stem)
- Control mechanisms do not require the cortex. Decerebrated animals
  - Cannot seek food
  - 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
  - LH needs inputs> Hunger and food intake are active processes
    - 2 types of neurons producing
  - melanin concentrating hormone (MCH)
  - Orexin (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
  - NeuroPeptide Y (NPY)
    - NPY injections in hypothalamus: eating frenzies. Rats will tolerate pain in order to eat> NPY increases motivation to eat
    - NPY from Arcuate nucleus (in hypothamua, near 3\textsuperscript{rd} ventricle)
    - NPY secretion is triggered by brain stem nuclei and controlled by stomach secretions (Ghrelin)
    - Endocannabinoids act NPY. Marijuana used to increases appetite in chemotherapy patients

Lateral hypothalamus/hunger summary

- Stomach (Ghrelin)/ brain stem (liver)> Arcuate (NPY)> lateral

Hypothalamus> increase eating/decrease metabolism

Hypothalamus

- 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 neurons inhibit the MCH/Orexin neurons via the MC-4R receptor
- Satiety
  - Leptin > NPY/ 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 disorders
  - An increasing problem: obesity > Diabetes
    - Type 1 diabetes: deficiency in insulin production (requires injections)
    - Type 2 diabetes: deficiency in insulin receptors (treated with pills)
- Ingestive behaviors: obesity
  - Average energy consumption
    - 20% muscles, 20% brain, 60% heat and digestion
  - Body weight: Energy stored - Energy 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 and above: Morbidly obese
    - Why 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 (1/3 of what we should be doing)
  - Overwriting of physiological signals for satiety: encourage to eat more, large portions
  - Availability of (bad) foods
- 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 diet)
  - Epidemiological studies (study of populations)
    - Pima Indians in the US vs Mexico
      - High metabolic rates > increases availability of calories
  - Spent if needed, stored if not

Ingestive behaviors: obesity
  - Mouse: obesity is due to leptin deficit
  - Humans: no evidence for leptin production deficits but:
Deficit in leptin transport through the BBB
Deficit in sensitivity of leptin
- Treatments
- Exercise
- 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
- Uncoupling protein (UCP). Convert nutrient to heat
- Conclusions:
  - Eat slowly
  - Eat regularly
  - Exercise (not too much)
  - Don’t eat at night

Anorexia Nervosa
- Definition
  - Refusal to maintain weight over the lowest weight considered normal for age/height
  - Intense fear of gaining weight or becoming fat
  - In women: three consecutive missed menstrual periods, without pregnancy
  - 80% of cases are young women. 15% death rate
  - Can be due to too much exercise (too much exercise decrease hunger signals). Restricting food results in increase physical activity (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 (evidenced by twin studies)
- Brain imbalance of NE, 5-HT AND NPY. No effective drug treatment

Treatment: psychotherapy