Brain Mechanisms: Evidence

- Hunger and satiety signals arise from the periphery and reach the brain
- Eating and drinking are evolutionarily ancient (involve the brain stem)
- Control mechanisms do not require the cortex
- Decerebrated animals (lesion)
  - 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

Lateral Hypothalamus

- Controls hunger
- Lesion -> decrease eating/drinking and body weight
- Stimulation -> increase eating/drinking
- Block glutamate transmission -> decrease food intake
- LH needs inputs -> hunger and thirst are active processes
- 2 types of neurons producing:
  - Melanin Concentrating Hormone (MCH)
    - Food deprivation increases MCH
    - Satiety decreases MCH
  - Orexin (aka hypocretin)
- Stimulation of MCH/orexin neurons
  - Increase appetite
  - Decreases metabolic rate
  - Increase motivation and movement
- MCH/orexin neurons project to areas involved in planning, motivation and movement

What triggers the LH MCH and Orexin neurons?

NeuroPeptide Y (NPY)

- NPY injections in the hypothalamus will trigger 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
  o Marijuana used to increase appetite in chemotherapy patients
• Stomach (Ghrelin)/Brain Stem (liver) -> Arcuate (NPY) -> Lateral Hypothalamus (MCH, orexin) -> increased eating, decreased metabolism

How do we stop eating?

Two parallel inhibitory pathways
• Leptin (from fat cells) inhibits NPY neurons in the Arcuate Nucleus
• Cocaine and Amphetamine Regulated Transcript (CART) neurons in the Arcuate Nucleus
  o CART neurons inhibit the MCH/Orexin neurons via the MC-4R receptor

Leptin
• Hereditary leptin deficiency (OB-like) in humans
  o Genetic deficit in production of leptin
• Leptin no longer used in weight loss diets; body becomes desensitized to leptin

Obesity
• Increasing problem: obesity -> diabetes
  o Obesity correlated with diabetes
  o Type 1 diabetes: deficiency in insulin production (required by injections)
  o Type 2 diabetes: deficiency in insulin receptors (treated with pills)
• Average energy consumption
  o 20% muscles
  o 20% brain
  o 60% heat + 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
  o 25-30: overweight
  o 30-40: obese
  o 40 and above: morbidly obese
• Why are people overweight?
  o On average: 2,500 kCal in and only 300 kCal out
  o Foods eaten are high in fat, sugar and calories
  o Not enough activity (1/3 of what is required)
Overwriting of physiological signals of satiety: encouraged to eat more, large portions

Availability of bad foods

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

  o Genetic factors: different metabolic rates
    ▪ Twin studies (high/low calorie diets)
    ▪ Epidemiological studies

  o Mice: due to leptin deficiency
  o Humans: no evidence for leptin deficits, but:
    ▪ Deficit in leptin transport through BBB
    ▪ Deficit in sensitivity of leptin receptors (MC4 receptors, age related)

  o In humans, high fat diets inherently decrease satiety signals
  o Night Eating Syndrome (NES): more Ghrelin and less leptin at night

• Treatment
  o Exercise (especially at a young age)
  o Wire In Jaw (close the mouth) and liquid diet
  o Gastroplasty: reshaping the stomach
  o Intestinal bypass: directly to the large intestine
  o Gastric bypass: 35% success in long-term decrease in weight, diminish secretion of Ghrelin (skip the stomach)
  o Gastric bubble
  o 5-HT promoters (relapse, cardiovascular side effects)
  o Uncoupling protein (UCP): convert nutrients to heat

• Conclusion
  o Eat slowly
  o Eat regularly
  o Exercise
  o Don’t eat at night

• Anorexia Nervosa
  o 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 (aged 15-24)
    - 15% death rate
  - Can be due to too much exercise (too much exercise decrease hunger signals)
    - Restricting food results in increased physical activity (and weight loss) Respond physiologically correctly to food -> not a loss of interest in food
    - >6 months starvation has psychological consequences (OCD?)
- Genetic factors (twin studies)
- Brain imbalance of NE, 5-HT and NPY
  - No effective drug treatment
  - Treatment: psychotherapy