“Ingestive Behaviors”

**Brain Mechanisms: Evidence**

- Hunger and satiety signals arise from the periphery and reach the brain
- Eating and drinking are evolutionarily ancient (i.e. involve the 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 $\Rightarrow$ decrease eating/drinking and body weight
  - Stimulation $\Rightarrow$ increase eating/drinking
  - Block glutamate transmission $\Rightarrow$ decrease food intake
  - LH needs input $\Rightarrow$ Hunger and food intake are active process
  - AP-5 =NMDA blocker
  - Injections of AP-5 decreases body weight
  - Placebo slight decrease of body weight
  - 2 types of neurons producing:
    - Melanin Concentration Hormone (MCH)
    - Orexin (aka 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 $\Rightarrow$ 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 $\Rightarrow$ MPY 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
  - **Stomach (Ghrelin) $\Rightarrow$ Arcuate (NPY) $\Rightarrow$ Lateral (MCH, Orexin) $\Rightarrow$ Increase Eating Brain Stem (liver) $\Rightarrow$ Hypothalamus $\Rightarrow$ Decrease Metabolism**
  - Ghrelin levels peak at meal times (breakfast, lunch, dinner, ‘night hunger’)

- **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 a-MSH) neurons inhibit the MCH/Orexin neurons via the MC-4R receptors
    - Satiety:
      - Leptin $\Rightarrow$ - NPY $\Rightarrow$ + MCH/ORexin
      - Leptin $\Rightarrow$ + CART $\Rightarrow$ - 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
- An increase problem: Obesity $\rightarrow$ Diabetes
  - Type 1 diabetes: deficiency in insulin production (requires injections)
  - Type 2 diabetes: deficiency in insulin receptors (treated in pills)
    - More common
- Southern USA has higher obesity $\rightarrow$ points to environmental factors
- Average energy consumption:
  - Muscles (20%), Brain (20%), Heat + Digestion (60%)
  - Bod weight $\leftrightarrow$ 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 & above: Morbidly obese (can lead to death without interference)
- 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 (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 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 $\rightarrow$ increase availability of calories $\rightarrow$ spent if needed, stored if not (hence obesity)
  - Low metabolic rates $\rightarrow$ no opportunity for fat storage (no obesity)
- Mouse: obesity is due to leptin deficit
- Human: no evidence for leptin production deficits, but:
  - Deficit in leptin transport through the BBB
  - 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
- 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 (USP)
  - Convert nutrient to hear

**Conclusion:**
- 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

- 80% of cases are young women
  - age: 15-20
  - 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 (evidenced by twin studies)
- Brain imbalance of NE, 5-HT and NPY.
  - No effective drug treatment
- **Treatment:** Psychotherapy