Chapter 11 – By Drema – 10/31

Brain Mechanisms: Evidence

- Hunger & 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/drink, can respond to hunger and thirst
  - Can differentiate different kinds of food
  - Can vomit/reject bad food: area postrema is intact

Figure 11.18

Hypothalamus

Lateral Hypothalamus

- Control hunger
- Lesion -> decrease eating/drinking and body weight
- Stimulation -> increase eating/drinking
- Block glutamate transition to LH -> decrease food intake

- AP-5 = NMDA Blocker
- LH needs inputs -> Hunger and food intake are active processes

- 2 types of neurons producing:
  - Melanin Concentrating Hormone (MCH)
  - Orexin (aka Hypocretin)

- Food deprivation increases MCH in LH satiety decreases NCH
- 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 cephalic ‘hunger’ variable? Figure 11.19
- What triggers the LH MCH and Orexin neurons?

Neuro Peptide 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 3rd ventricle)
- NPY secretion is triggered by brain stem and controlled by stomach secretions (Ghrelin)
- Endocannabinoids act like NPY. Marijuana used to increase appetite in Chemotherapy patients.
- Figure 11.20 Ignore- Paraventricular nucleus, AGRP
- Figure 11.12
**Lateral Hypothalamus/Hunger Summary**

- Stomach (Ghrelin)
- Arcuate (NPY)
- Lateral (MCH, Orexin)
- Hypothalamus

**Brain Stem (liver)**
- 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-4 receptor

**Satiety:**

- Leptin inhibits NPY neurons
- CART neurons inhibit MCH/Orexin neurons

*Figure 11.21*

**Leptin**

- Hereditary Leptin Deficiency (OB-Like) in humans
  - Genetic deficit in the production of Leptin
- Leptin no longer used in weight loss diets
  - Lead to Leptin resistance

**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)
- Average energy consumption
  - Muscles - 20%
  - Brain - 20%
  - Heat & Digestion - 60%
    - 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+ = Morbidly Obese
- Why are people overweight?
  - On average, 2500 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
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 U.S. 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
    - No obesity
- **Mouse**- Obesity is due to Leptin deficit
- **Human**- No evidence for Leptin production deficit, 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
- Night Eating Syndrome (NES): More Ghrelin and less Leptin at night

**Treatments**

- Exercise (especially at a young age)
- Wire in jaw (close the mouth) & liquid diet
- Gastroplasty- Reshaping the stomach
- Intestinal bypass (directly into the large intestine)
- Gastric bypass- 35% success in long-term decrease in weight
  - Diminish the 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!
- Figures 11.24 & 11.25

**Ingestive Behaviors: Anorexia Nervosa**

- **Definition**
  - Refusal to maintain weight over the lowest weight considered normal for age/weight
  - 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), with a 15% death rate
• Can be due to too much exercise (too much exercise decreases hunger signals)
  o Restricting food results in increase physical activity (and weight loss)
• Respond physiologically correct to food -> Not a loss of interest in foods
• In normal, >6 months starvation has psychological consequences
• Genetic factors (evidenced by twin studies)
• Brain imbalance of NE, 5-HT, and NPY. No effective drug treatment
• Treatment: Psychotherapy
• Figure 11.26

Ingestive Behaviors: Hunger
• Lipoprivic hunger
  o Injection of drugs that blocks fatty acid metabolism
    ▪ Hunger
  o Lesion of Vagus nerve -> bocks hunger
• Liver & Vagus nerve monitor glucose & fat levels & send signals to brain to signal hunger
  o Start meal

Ending a Meal -Satiety
• Anticipatory
  o Gastric Factors- Nutrient receptors in stomach. Stretch receptors in stomach
  o Intestinal Factors-Detection of fat in duodenum, CCK
    ▪ Stomach (decrease outflow)
    ▪ Bile (Increase fat breakdown)
    ▪ Brain (‘Stop’ signal via Vagus nerve)
  o PYY released by the duodenum after a meal
    ▪ Proportional to calories ingested
  o Injections of PYY provides a satiety signal
• Liver Factors- Glucose receptors-> Satiety signal in brain via Vagus nerve
• Pancreatic Factors- Absorptive phase. Insulin -> Insulin receptors in brain
• Cephalic (Cognitive) Factors- Learning to identify rich food

Long Term Satiety- Fatty Storage Factors
• Leptin secreted by fat cells, increase fat metabolism
• OB Mouse- Leptin deficient
• Injecting Leptin-> Smaller meals
  o Leptin is a (fat related) satiety signal