Ingestive Behavior
(i.e., eating and drinking)
Chapter 11
Part 2: Hunger
How the Brain Works (Simplified)

BRAIN

\[ \text{ADP} \rightarrow \text{ATP} \rightarrow \text{energy} \]

\[ \text{glucose} \rightarrow \text{CO}_2 + \text{H}_2\text{O} \]

\[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{carbohydrates} \rightarrow \text{glucose} \rightarrow \text{glycogen} \]

\[ \text{LIVER} \]

\[ \text{photosynthesis by green plants} \rightarrow \text{carbohydrates} \rightarrow \text{animals} \]

\[ \text{O}_2 \rightarrow \text{sunlight} \rightarrow \text{climate} \rightarrow \text{H}_2\text{O} \]

\[ \text{birds keep insects in check} \]

\[ \text{pollination by insects} \]

\[ \text{action of root system on soil} \rightarrow \text{soil} \rightarrow \text{parent material (limestone, granite)} \rightarrow \text{climate} \]

\[ \text{decomposers (fungi, molds, bacteria, earthworms, beetles, centipedes, etc.)} \]

\[ \text{soil preparation (moles, shrews, root systems, etc.)} \]

\[ \text{erosion by water (ice) and pioneers (lichens)} \]

\[ \text{N}_2 \text{ (air)} \rightarrow \text{legumes} \]
Nutrition (the short course)

- Eating incorporates into our bodies atoms and molecules that were once part of the bodies of other organisms (plants and animals).
- 99% of dry body mass is made up of four elements
  - carbon - derived ultimately from air
  - oxygen - derived ultimately from air
  - hydrogen - derived ultimately from water
  - nitrogen - derived ultimately from soil
- Plants biosynthesize these elements into complex biological molecules, using sunlight as a source of energy.
- When we digest these molecules, we liberate the energy from sunlight that the plants had incorporated into the chemical bonds.
  - and store it in the high-energy phosphate bonds of ATP
  - when we need it to run membrane pumps and so forth: ATP $\rightarrow$ ADP + energy
Nutrition (the short course)

Diagram:
- **Oxygen (O₂)**
  - Carbohydrates → Glucose → Glycogen (Liver)
  - Photosynthesis by green plants
- **Glucose → CO₂ + H₂O** in the Brain
  - ADP → ATP → Energy
- **Animals** receive carbohydrates from green plants through photosynthesis.
Nutrition (the short course)

- Two hormones regulate the storage of glucose in the liver (and elsewhere) as glycogen.

Fig. 11.9
Nutrition (the short course)

- nutrients in food - i.e., the system variables for hunger
  - vitamins and minerals - minor nutrients
  - carbohydrates (starches and complex sugars)
    - broken down into glucose (and other sugars)
    - and used for energy metabolism
    - or stored as glycogen in the liver
    - or converted to and stored as fat
  - requirement - about 100g/day to prevent ketosis and protein breakdown (muscle wasting)
- proteins - next slide...
Nutrition (the short course)

- nutrients in food - i.e., the system variables for hunger
  - proteins
    - broken down into amino acids
    - which can be converted to
      - glucose
      - fatty acids
    - or used for the biosynthesis of peptides and proteins
      (hormones, neurotransmitters, enzymes, receptor sites, ion channels, membrane pumps, etc.)
  - requirement - 0.8-0.9g/kg of body weight per day
Nutrition (the short course)

• nutrients in food - i.e., the system variables for hunger

• fats (triglycerides)
  • broken down into glycerol (which is converted to glucose) and fatty acids
  • which can be used for energy metabolism by the body (but not the brain)
  • can be converted to ketones for energy metabolism by the brain - ketosis
  • or can be stored as triglycerides in fat cells (adipose tissue)

• requirement - some fatty acids are essential (i.e., must be obtained in the diet)
Brain Metabolism

- The brain is metabolically very active.
- When the body is at rest, the brain is the most expensive tissue in the body to supply with energy.
- When the body becomes active, muscles become much more expensive (about 50 cal/sec or 200 watts during strenuous exercise).
- A 70 kg (154 lb) man needs about 1600 kcal/day to sustain his body (BMR). Note: 1 kcal = 1 nutritional Calorie.
  - 18 cal/sec or 75 watts - same as a typical incandescent bulb in a lamp
  - 4 cal/sec is used by the brain, or about 15 watts (350 kcal/day)
    - a little less than half of that goes into maintaining neurons
  - 7 watts - same as a Christmas light (one of the large ones)
Eating

• hunger - eating must be turned on before the body begins to starve

• satiety - eating must be turned off before nutrients have a chance to reach tissues

• homeostasis - some system variable (or variables) is monitored and compared to a set point
Conscientious Objector Study (WWII)

- COs volunteered to be starved - caloric intake cut to 50% of maintenance for 6 months
  - body weight fell to 75% of baseline, less than predicted
  - reduced activity - sat around whenever possible
  - BMR dropped - adaptive thermogenesis
  - semistarvation neurosis
    - began to think and talk incessantly about food
    - became less sociable
    - lost interest in sex and girlfriends
    - became depressed and irritable
  - when finally allowed free access to food - showed strong preference for high Calorie foods like cake and ice cream (same foods irresistible to dieters - no one ever binges on broccoli)
Vermont State Prison Study (1966)

- got volunteers to overeat by 1000 Cal/day
- BMR rose by 10% - adaptive thermogenesis
- some had great difficulty gaining weight because of this
- adaptive thermogenesis did not occur in people who were already overweight
Summary

- When free-feeding, we take in Calories sufficient to maintain body weight at a set point.
- When the quality of the diet is changed, we will change how much we eat (making dieting tricky).
- If Calories are deficient or too abundant, other mechanisms kick in to compensate, such as adaptive thermogenesis.
- The basic formula still holds for maintaining a constant body weight: calories in = calories out.
Two Phases of Metabolism

- fasting phase - pancreas stops secreting insulin and begins secreting glucagon
  - glycogen to glucose
  - triglycerides to fatty acids and glycerol
  - fatty acids used for energy metabolism by the body
  - glucose spared for the brain

- absorptive phase - pancreas stops secreting glucagon and begins secreting insulin
  - glucose to glycogen (glucose is stored)
  - fatty acids to triglycerides (fats are stored)
  - glucose used for energy metabolism in both brain and body
Two Phases of Metabolism

Figure 11.10
Starvation

- Glycogen stores in the liver are sufficient to last about one day.
- Fatty acids are converted to ketones to be used for energy metabolism in the brain.
  - keto-acidosis or ketosis
  - “fruity” breath
  - ketones bind Na in the blood, which is then excreted
  - excess carbon dioxide formed in the blood
  - blood becomes too acidic - leads to mental changes
    - depression
    - lethargy
    - coma
What Starts a Meal?

• ghrelin - a peptide hormone released from the stomach when it is empty
• feelings of hunger are correlated with blood levels
• IV injection in humans
  • stimulates food intake
  • elicited vivid images of subjects’ favorite foods
• filling of the stomach inhibits ghrelin release (whereas injections of nutrients into the blood do not)
• release is controlled by receptors in the duodenum
• mice without the ghrelin gene or gene for its receptors eat normally and maintain normal body weight - there is more to hunger than ghrelin

Figure 11.11-like
Levels of ghrelin in human blood plasma

What Starts a Meal?

- metabolic signals
  - glucoprivation - depriving cells of glucose
    - hypoglycemia - low blood glucose
    - 2-DG injections - completes with glucose for uptake
  - lipoprivation - depriving cells of lipids (fats)
- two sets of receptors for nutrients
  - one in the brain - detect glucoprivation
  - one in the liver - detect both gluco- and lipoprivation
What Starts a Meal?

- metabolic signals (cont.)
  - Novin, VanderWeele, & Rezek (1973) - infused 2-DG into the hepatic portal vein
    - stimulated immediate eating
    - cutting the vagus nerve prevented this
  - Ritter & Taylor (1990) - same result from inducing lipoprivation in the liver
  - Ritter, Dinh, & Zhang (2000) - infused 5-TG (similar to 2-DG) into two regions of the medulla
    - induced eating - the brain has its own receptors
  - Tordoff, Hopfenbeck, & Novin (1982) - cutting the hepatic branch of the vagus nerve, which sends info to the brain from the liver, has little effect on an animal’s day-to-day eating
What Stops a Meal?

• short-term satiety signals

• head (sensory) factors - play a role in learning

• gastric (stomach) factors - the stomach contains nutrient receptors (stomach stretch does not play much of a role, ordinarily!)

• intestinal factors

  • there are glucose, amino acid, and fatty acid receptors in the duodenum

  • in addition there are several possible hormonal signals - decrease in ghrelin secretion from the stomach, secretion of CCK from the duodenum in response to fats, secretion of peptide PPY from the gastrointestinal tract in response to ingested nutrients, and secretion of insulin from the pancreas

• liver factors (the first organ to learn that nutrients are being absorbed from the intestines) - both glucose and fructose (which does not cross the BBB) infused into the hepatic portal vein inhibit eating (Tordoff & Friedman, 1988)
What Stops a Meal?

• long-term satiety signals

• adipose tissue - the leptin story
  • ob mice - a strain of mice that have low metabolism, overeat, become exceedingly fat, and often develop diabetes in adulthood
  • have an abnormal OB gene
  • prevents the secretion of leptin (a peptide hormone) from fat cells - fat cells normally secrete leptin when they are “well nourished”
  • ob mice given daily injections of leptin return to a normal body weight
  • there is a condition in humans called hereditary leptin deficiency - people with this condition are usually obese
  • leptin cannot be used to treat obesity in most humans because leptin levels are already about 300% of normal - obese people are leptin resistant
Brain Mechanisms In Hunger

- since ingestion is a very primitive behavior, we might expect it to be regulated in the lower brainstem
  - this is where the brain receives sensory info about taste - nucleus of the solitary tract via the facial and glossopharyngeal nerves
  - there are also nutrient (glucose) receptors here
  - but in “higher animals” this information is relayed into the upper brainstem and telencephalon
Hypothalamus

- classic studies
  - lateral hypothalamus or LH (Anand & Brobeck, 1951)
    - lesions cause rats to stop eating
    - electrical stimulation causes rats to eat
  - ventromedial hypothalamus or VMH (Hetherington & Ranson, 1942)
    - lesions cause rats to eat themselves into obesity
    - electrical stimulation stops eating
Hypothalamus

- So what role do these structures play in the regulation of food intake?
  - VMH - ???
  - LH - secretes orexigenic peptides or orexigens that stimulate hunger and decrease metabolic rate
    - melanin-concentrating hormone (MCH)
    - orexin (hypocretin)
Hypothalamus

Figure 11.18
Feeding Circuits in the Brain
• So what controls the LH?

• neuropeptide Y (NPY) released from the arcuate nucleus of the hypothalamus

• causes frantic, ravenous eating when infused into the brain

• is also released from glucose sensitive neurons in the medulla

• agouti-related peptide (AGRP) - also released from the arcuate nuc.

• endocannbinoids also increase release of orexigenic peptides from the LH

• The arcuate nuc., in turn, receives input from NPY neurons in the medulla, which respond to glucoprivation, and has ghrelin receptors.
Hypothalamus

• role in long-term satiety

• the NPY/AGRP neurons of the arcuate nuc. also contain leptin receptors

• leptin has an inhibitory effect on these neurons

• the arcuate nuc. also releases two anorexigenic peptides that inhibit eating - release of these is stimulated by leptin

• CART

• alpha-MSH
So What About The VMH?

1) receives info about leptin, insulin, and glucose through neural input as well as via the CSF (3rd vent.)

2) sends glutaminergic (excitatory) output to the satiety center in the arcuate nucleus

3) rats with VMH lesions have increased blood glucose and increased blood leptin levels - but they don't seem to be able to make use of this info to regulate food intake

Note: POMC  \[\xrightarrow{\text{precursor peptide}}\] alpha-MSH
Eating Disorders

• There are a lot of mights and maybes here...

• but very little definite knowledge.
The end of eating.