Hunger

WEEK 9, LECTURE 3

Instructor: Erin Horowitz

To finish up the lecture series for this week, let's talk about hunger.

Hunger

Animals vary in their eating strategies

- Predators have large digestive systems adapted to huge, infrequent meals
- Bears eat constantly
- Small birds eat only what is needed at the moment (preserves light weight for flight)
- Chickadees eat enough daily to increase body weight 10 percent
  - Then lose it at night keeping warm

Broadly defined, hunger is a motivational state that drives organisms to consume food, which supplies the body with energy and other nutrients to carry out its essential processes.

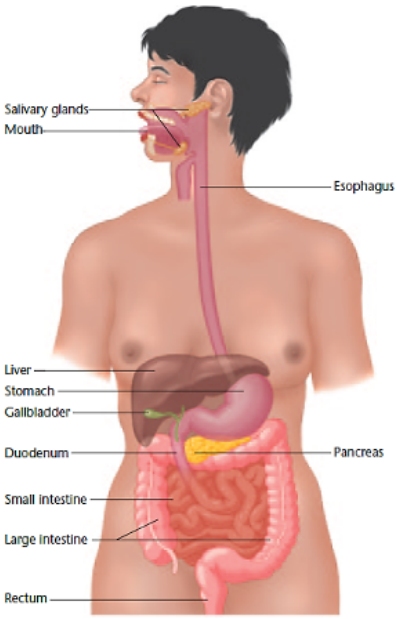
All animals experience hunger, but they differ widely in their eating strategies. You can read about some of these strategies above. As you read through, I'd like you to think about the relative size of these different animals, and how much energy their bodies would need to function. Eating is tied to energy consumption.

Digestion and Food Selection

Digestive system function
- Breaks down food into smaller molecules that the cells can use

Digestion begins in the mouth
- Enzymes in saliva break down carbohydrates

Hydrochloric acid and enzymes in the stomach digest proteins



In all animals, the consumption of food is controlled by the digestive system. The broad function of this system is to break down food into smaller components, which can then be used by cells to perform necessary body processes.

Digestion actually starts in the mouth. Saliva contains enzymes that break down food – especially carbohydrates. From there, food moves to the stomach, where hydrochloric acid and different enzymes digest proteins.

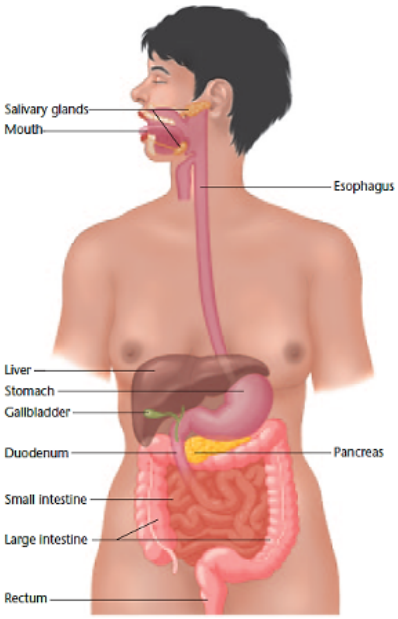
Digestion and Food Selection: The Intestines

Enzymes in the small intestine digest proteins, fats, and carbohydrates

- Digested food absorbs into the bloodstream

The large intestine absorbs water and minerals

- Lubricates the remaining materials to pass as feces



From the stomach, food moves into the intestines. In the small intestine, enzymes digest proteins, fats, and what's left of the carbohydrates. All of the food digested here moves through the walls of the intestine and into the blood stream.

Finally, food moves into the large intestine, which absorbs any remaining minerals and water. Anything we don't need at that point is excreted as feces. Digestion is, overall, an incredibly efficient process.

Consumption of Dairy Products

At the age of weaning, most mammals lose the intestinal enzyme **lactase**, which is necessary for metabolizing **lactose** (the sugar found in milk)

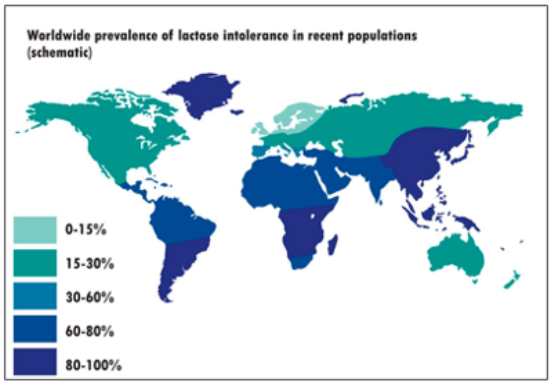
Milk consumption after weaning can cause gas and stomach cramps

Declining levels of lactase may be an evolutionary mechanism to encourage weaning

Many human adults have enough lactase to consume milk and other dairy products throughout their lifetime

Nearly all adults in China and surrounding countries lack the gene that enables adults to metabolize lactose

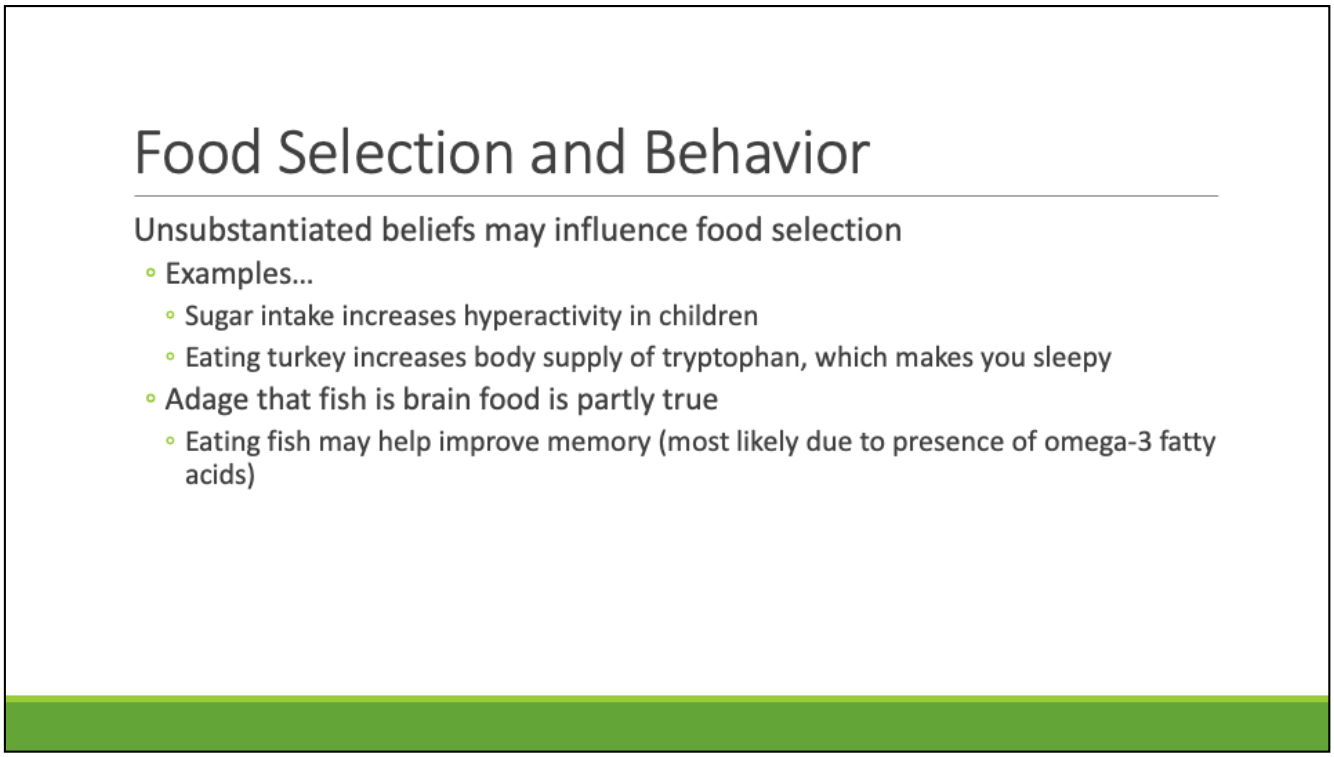
- Only small quantities of dairy products can be consumed



From Wikipedia Commons (2013)

This is a bit of a tangent, but there's an interesting case of eating and digestion which involves the consumption of dairy products – mainly, lactose intolerance. You can read through the slide for more information.

People who are able to consume dairy products can likely do so because their ancestors domesticated cattle. This was more common in places like Europe and parts of Africa, and less so in places like China – hence the larger percentage of lactose intolerance in that area.



There are also a lot of myths surrounding why we eat the things we eat… for example, the idea that sugar intake increases hyperactivity in children. This is patently false; studies that have looked at children's sugar consumption found no increase in activity after eating a sugary snack, compared to a sugarless snack.

Similarly, while it's true that tryptophan can increase melatonin production, you can't really consume enough of it through eating turkey for it to have a significant effect. It's more likely that people get sleepy on Thanksgiving because they eat a lot in general, and eat a lot of carbs in particular. Carbs increase insulin production, and insulin pushes other amino acids out of the way, which clears the way for tryptophan to enter the brain.

On the other hand, there is some credence to the idea that fish is "brain food," although this is still an area of active research.

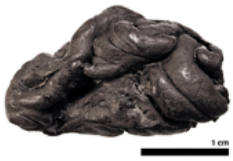
Short- and Long-Term Regulation of Feeding

Oral factors

- The desire to taste and chew are also motivating factors in hunger and satiety
- Humans have been chewing gum since 4500 B.C.

Evidence from **sham-feeding experiments**

- Everything an animal eats leaks out of a tube connected to the stomach or esophagus
- Do not reliably produce satiety

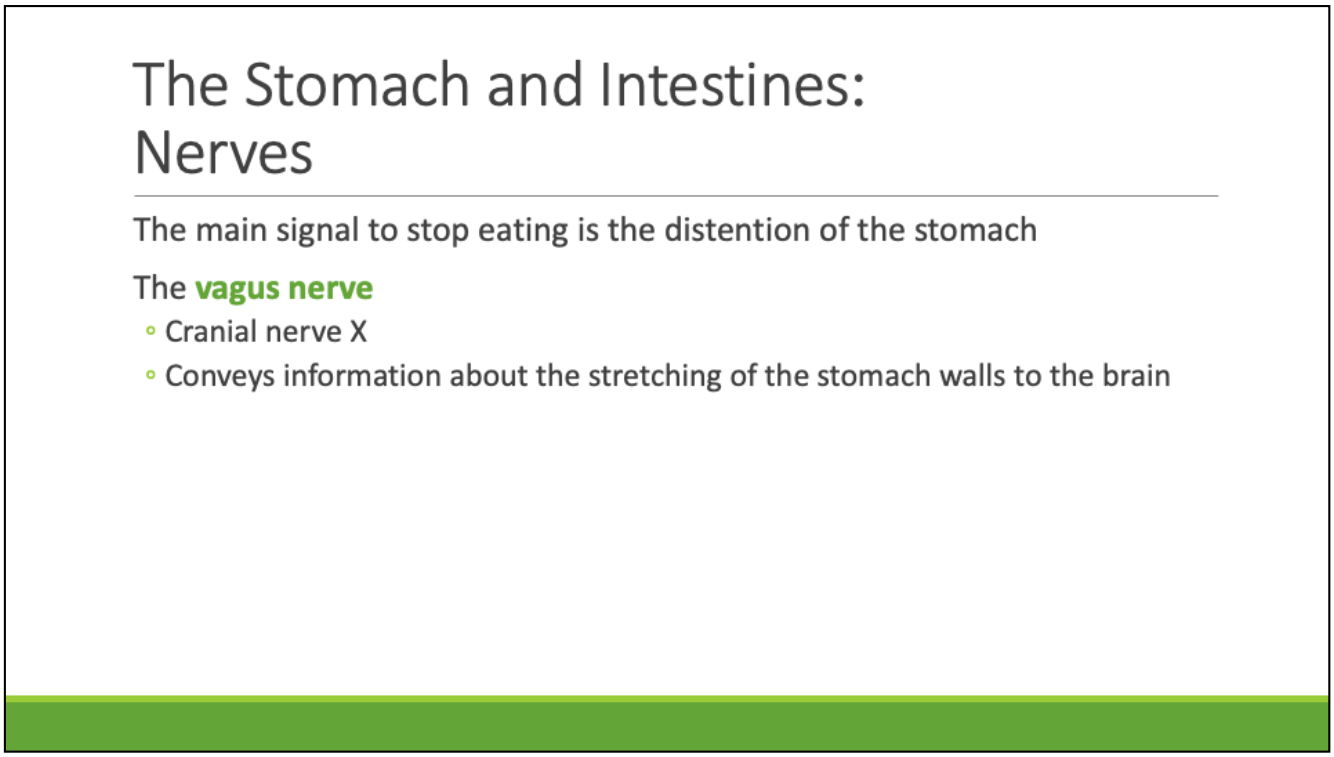


Neolithic chewing gum (5700 years old)

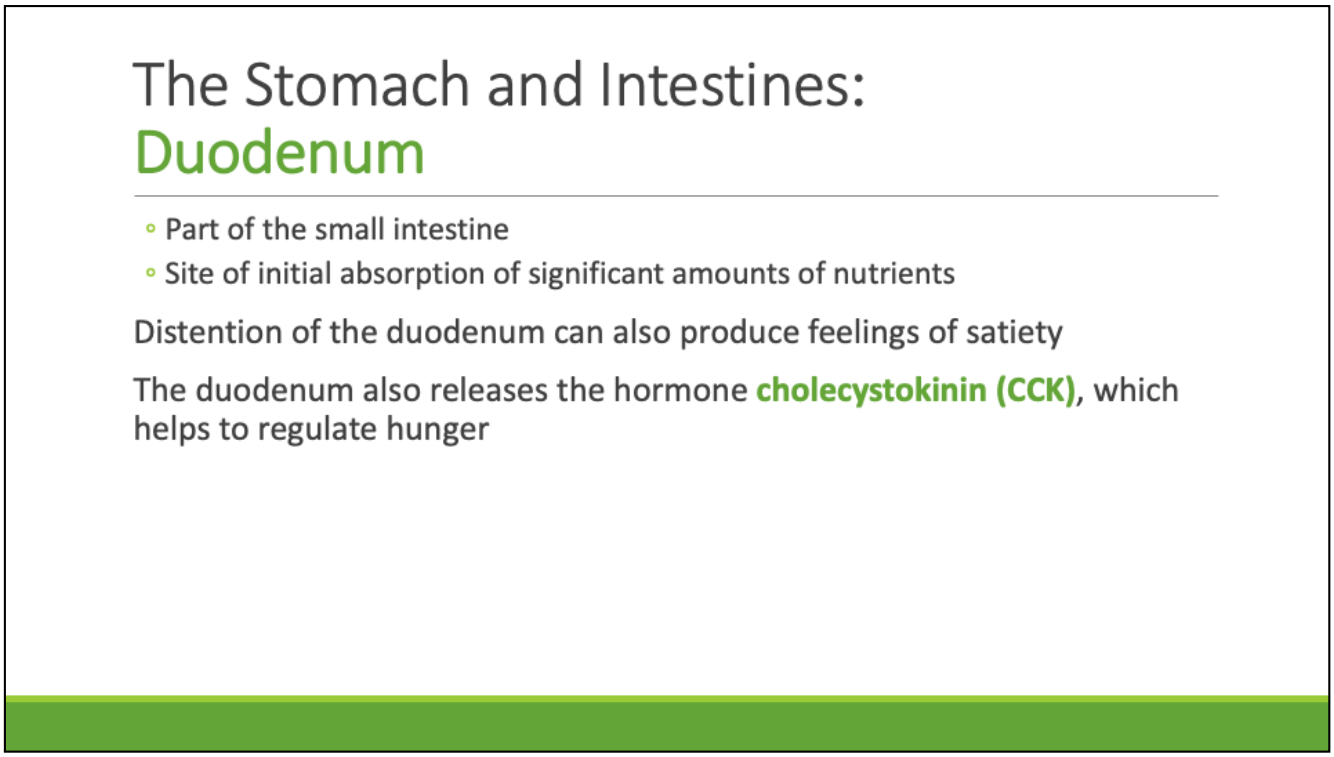
Feeding behavior is regulated by a number of different factors and different areas of your brain and body. For example, we have oral factors which actually increase the sense of reward you get from eating.

These oral factors are important → your book describes a study in which students were basically fed through feeding tubes for a week, and while they reported feeling satiated (i.e., full), they also reported having a strong desire to taste or chew something.

On the other hand, animals that are able to chew their food but then have a tube that shunts the food out of their bodies will eat almost continually. So taste is important, but it does not significantly contribute to the feeling of being full.



Much like with thirst, satiety is measured by the distention of the stomach. This information is communicated by one of the cranial nerves – the vagus nerve (or cranial nerve X) – which travels from the brain all the way down to the stomach. This nerve essentially "measures" the stretching of the stomach, and communicates that information to the brain, which will then signal a stop to the feeling of hunger (given that the stomach is full enough, of course).



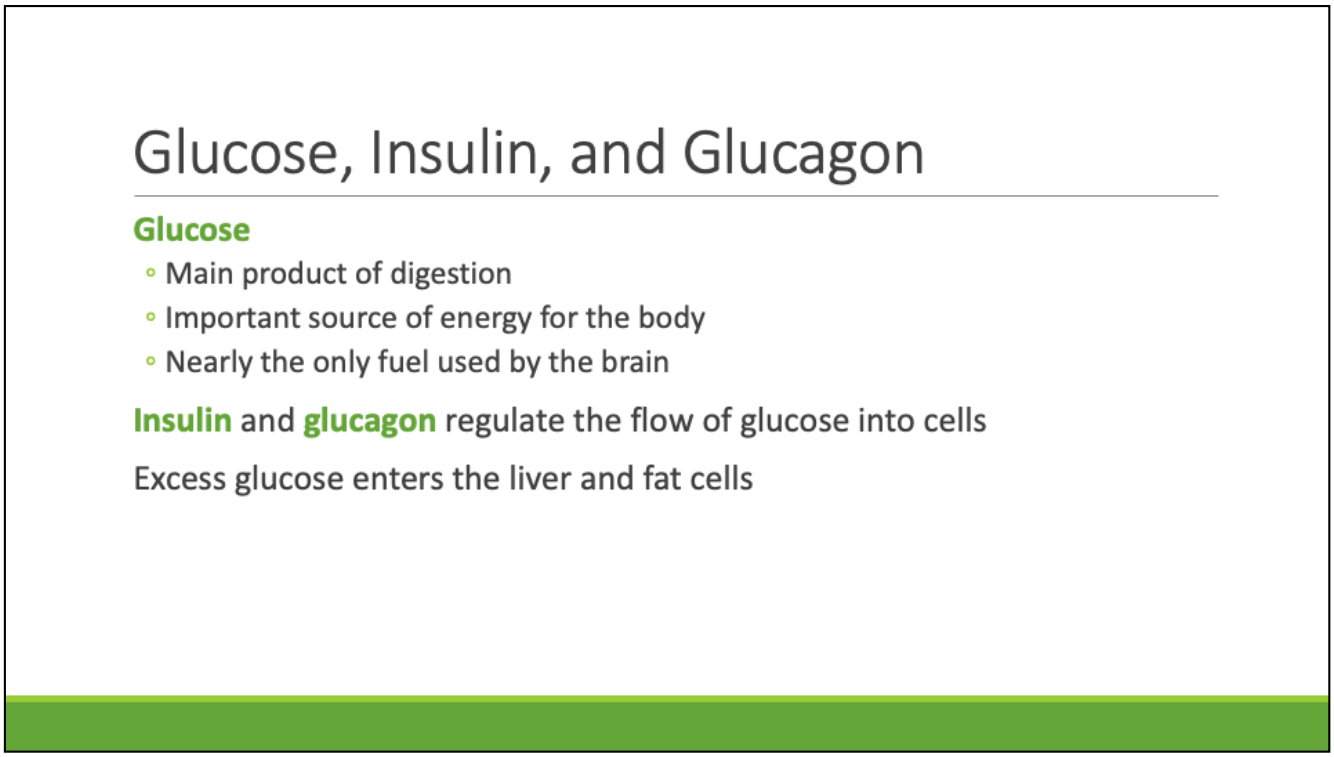
In addition to the vagus nerve, there's another structure called the duodenum that contributes to feelings of satiety. This area is part of the small intestine, and it's actually where the majority of nutrients are absorbed during digestion. The duodenum measures distention of the small intestine and releases a hormone called cholecystokinin (CCK for short), which can contribute to a sense of fullness.

The Stomach and Intestines: CCK

Cholecystokinin (CCK) released by the duodenum regulates hunger by…

- Closing the sphincter muscle between the stomach and duodenum and causing the stomach to hold its contents and fill faster
- Stimulating the vagus nerve to send a message to the hypothalamus that releases a chemical similar to CCK

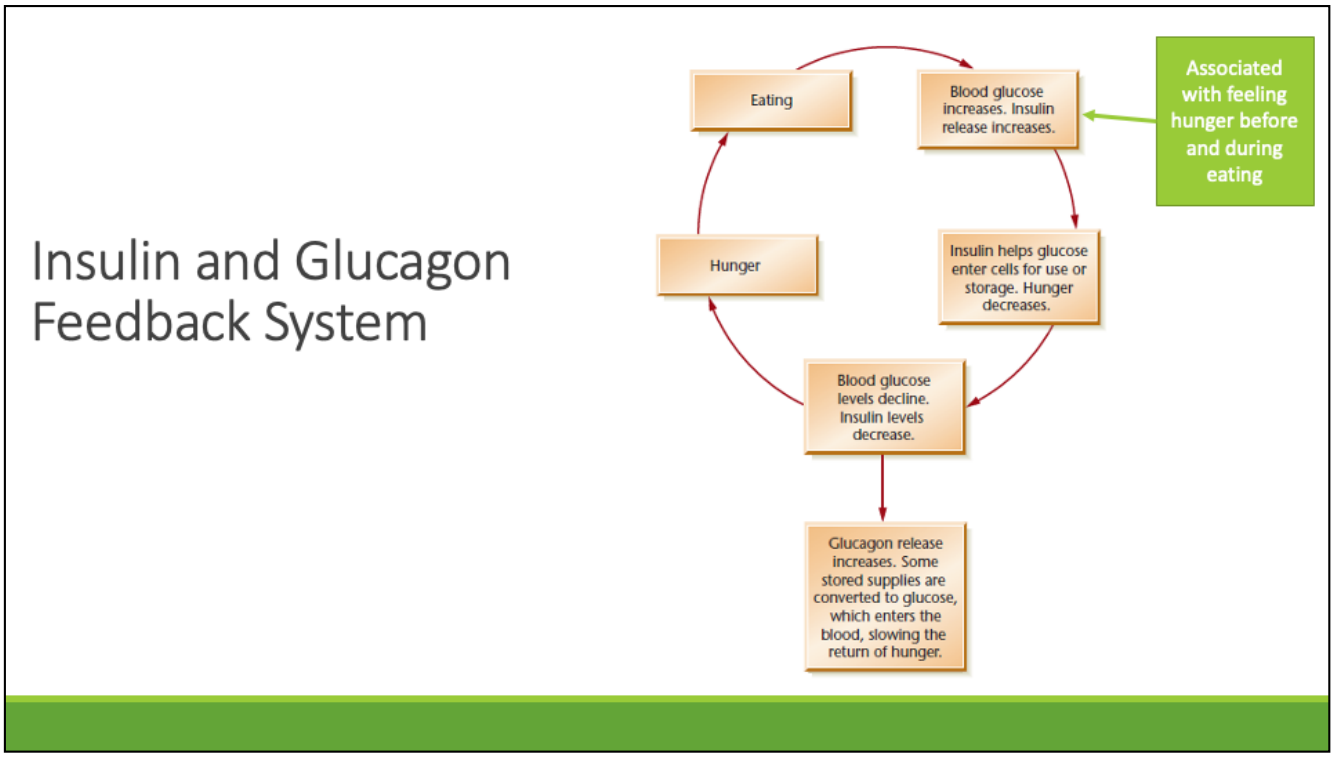
Let's actually talk a little more about CCK. How, exactly, does it regulate hunger? You can read more about this in the slide above.



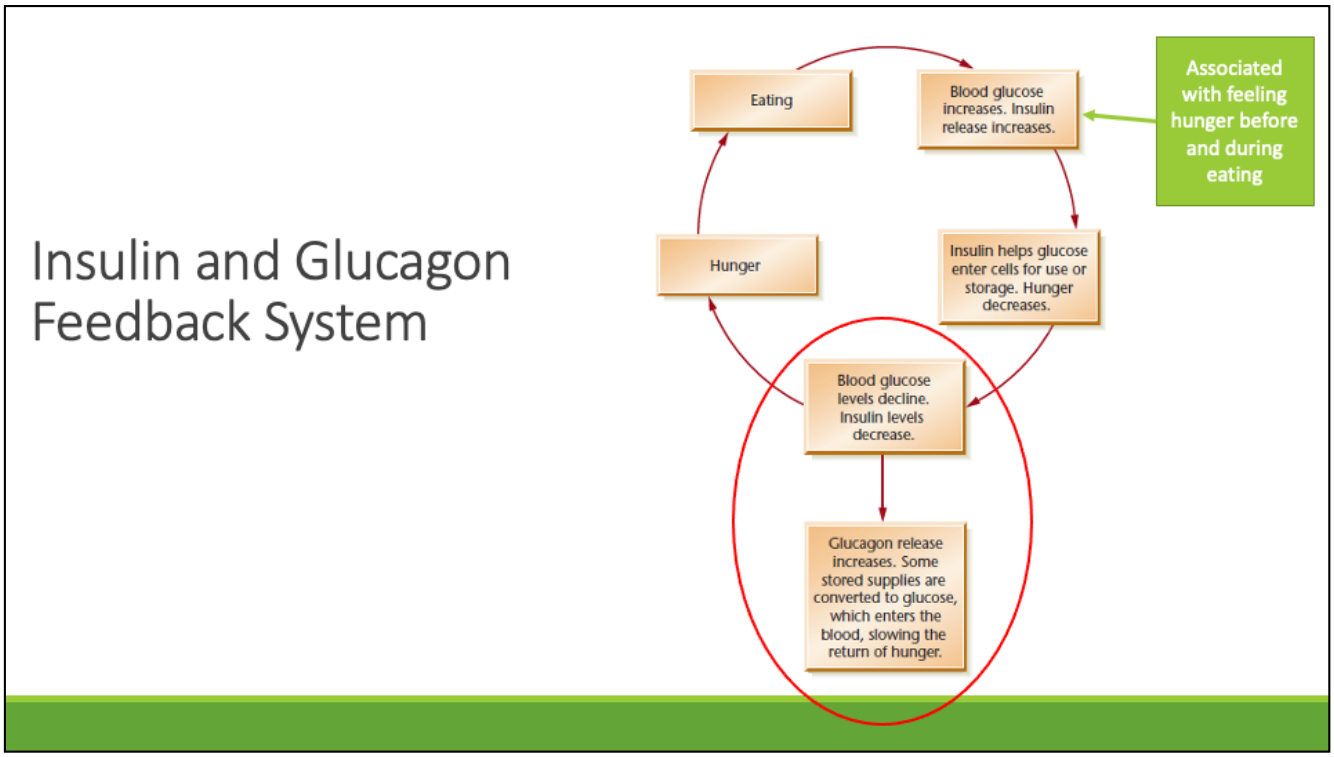
So that is, generally, how satiety is regulated via the stomach. Let's zoom in a little now and talk about some of the components that are involved in this process: mainly, glucose, insulin, and glucagon. We'll start with a broad description and move from there to a discussion of how they all work together.

Most of the food you eat gets converted into glucose. It's the main product of digestion, a primary source of energy for the body, and the only fuel used for brain processes.

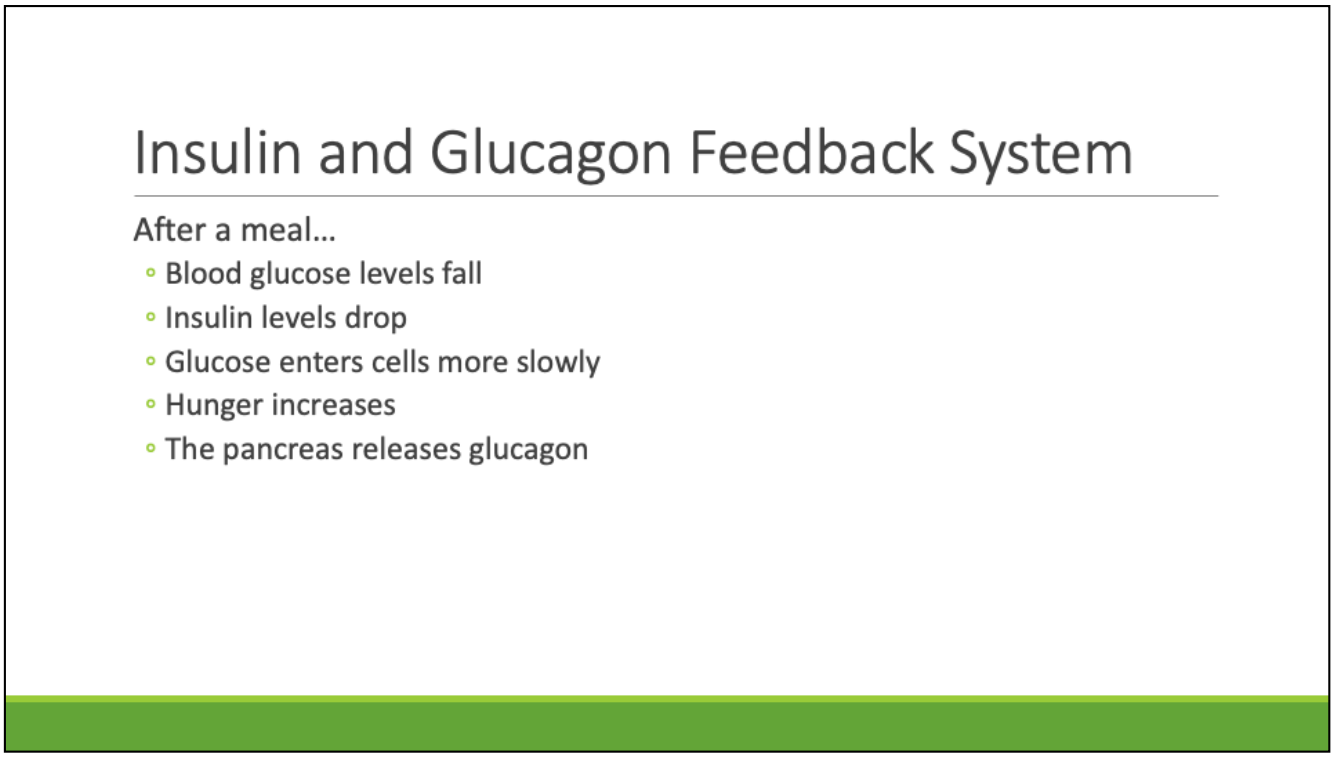
Insulin and glucagon are pancreatic hormones that regulate the flow of glucose into the cells to aid with various bodily processes. Any glucose that does not get used is stored in the liver, and in fat cells.



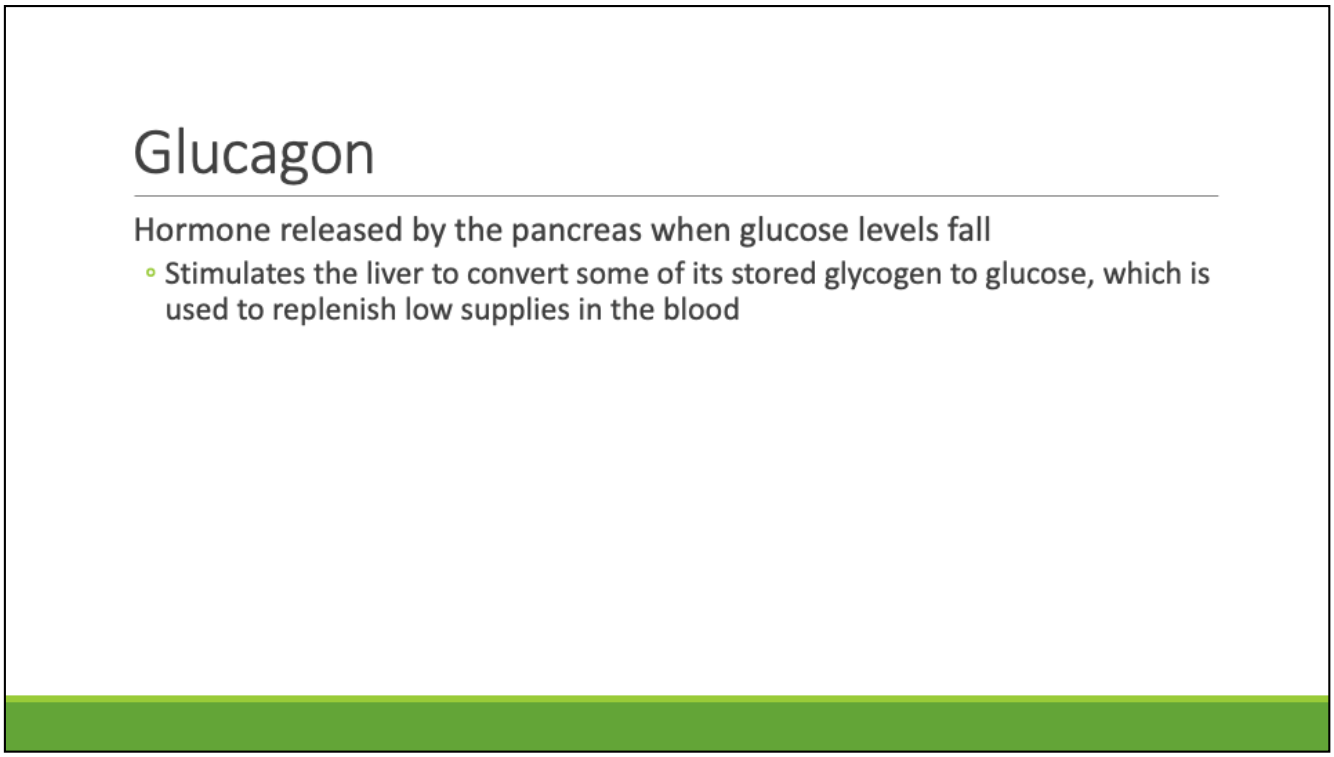
These three components work together to produce a cycle of hunger and satiety. This is how it all plays out: When you feel hungry, you eat, and glucose levels rise (both before and during eating). This causes the pancreas to release insulin, which helps glucose enter cells. When glucose enters cells, this suppresses hunger and decreases eating, which in turn lowers glucose levels until the body experiences hunger again.



This part of the cycle is worth looking at a little more closely, which we'll do on the next slide…



After eating, and after insulin moves glucose into the cells, both glucose and insulin levels drop (glucose because it's being used, and insulin because it's no longer needed). As a result of the drop in insulin, the movement of glucose into cells slows down… and with that, comes an increase in hunger (to motivate an individual to supply the body with more of it). As this is happening, the pancreas releases glucagon…

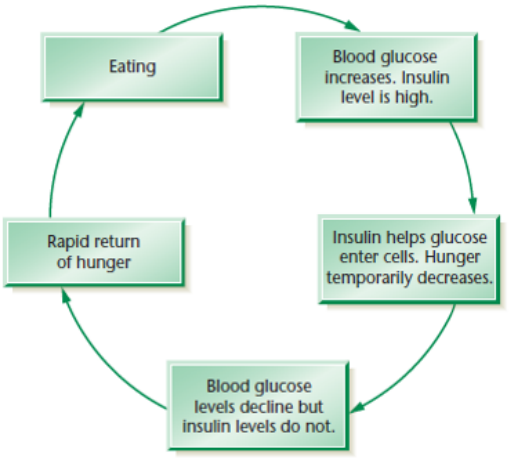


… we haven't talked much about glucagon yet, but broadly, it's a hormone that's released by the pancreas at the point when glucose levels decrease. Glucagon essentially triggers stored glucose to start being used by the body - you can read about this in more detail above.

Insulin Levels

If insulin level stays constantly high:

- The body continues rapidly moving blood glucose into the cells long after a meal
- Blood glucose drops and hunger increases in spite of high insulin levels
- Food is rapidly deposited as fat and glycogen
- Causes weight gain
  - Valuable preparation for winter in some animals



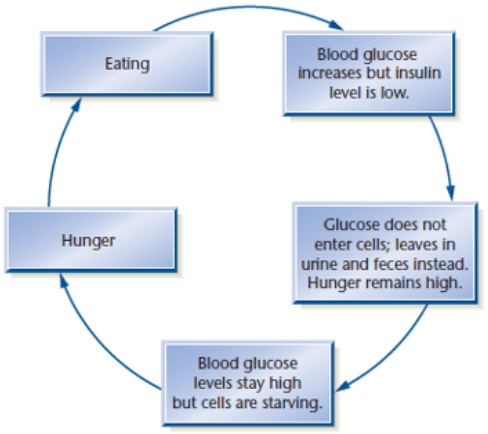
There are some cases – say, when overeating, when insulin levels maintain a consistently high level. You can read about the consequences of this above. Notice how this changes the cycle we've been discussing.

When this happens, blood glucose is continually stored as fat and glycogen. It becomes increasingly difficult to mobilize the stored nutrients, and because of that it's easier to become hungry even after eating (the body does not see the stored nutrients as available for use, so it triggers a hunger state to acquire more). The consequence of this is weight gain, which is good for some animals but can be harmful for others.

Type I Diabetes

In people with Type I diabetes, insulin levels remain constantly low, but blood glucose levels are high

- People eat more food than normal, but excrete the glucose unused and lose weight
- Cycle of untreated Type I Diabetes →



Type 1 diabetes is a condition that affects insulin and glucose levels. More specifically, with this condition, insulin levels are consistently low, but blood glucose levels are high. You can read about the consequences for this in the slides above. Notice again how these two factors alter the cycle.

Because of low insulin levels, the glucose in the blood can't enter the cells, either to be stored or to be used. And so individuals with Type I diabetes end up excreting glucose in their urine while their cells are starving, which could be incredibly harmful.

Leptin

Long-term hunger regulation is accomplished by the monitoring of fat supplies by the body

The body's fat cells produce the peptide leptin, which signals the brain to increase or decrease eating

Low levels of leptin increase hunger

High levels reduce eating and increase physical and immune system activity

High levels of leptin do not necessarily decrease hunger

- Obesity is associated with a lower sensitivity to leptin
- Sensitivity declines during pregnancy and when animals prepare for hibernation

Puberty is triggered by a certain level of leptin during adolescence

So far we've been talking about short-term sensations of hunger: for example, throughout the day we experience cycles of hunger and satiety.

Now the question is: how does the body regulate more long-term sensations of hunger? How do we know if we are in a critical state of hunger (i.e., starvation), for example?

This is regulated largely by a peptide called leptin, which you can read about above.

Brain Mechanisms of Hunger

Information from all parts of the body regarding hunger impinge onto the **arcuate nucleus**

The arcuate nucleus is a part of the hypothalamus containing two sets of neurons…

- Neurons sensitive to hunger signals
- Neurons sensitive to satiety signals

Okay, so that does it for short-term and long-term sensations of hunger. Let's move on and talk about what happens in the brain when hunger and satiety are triggered.

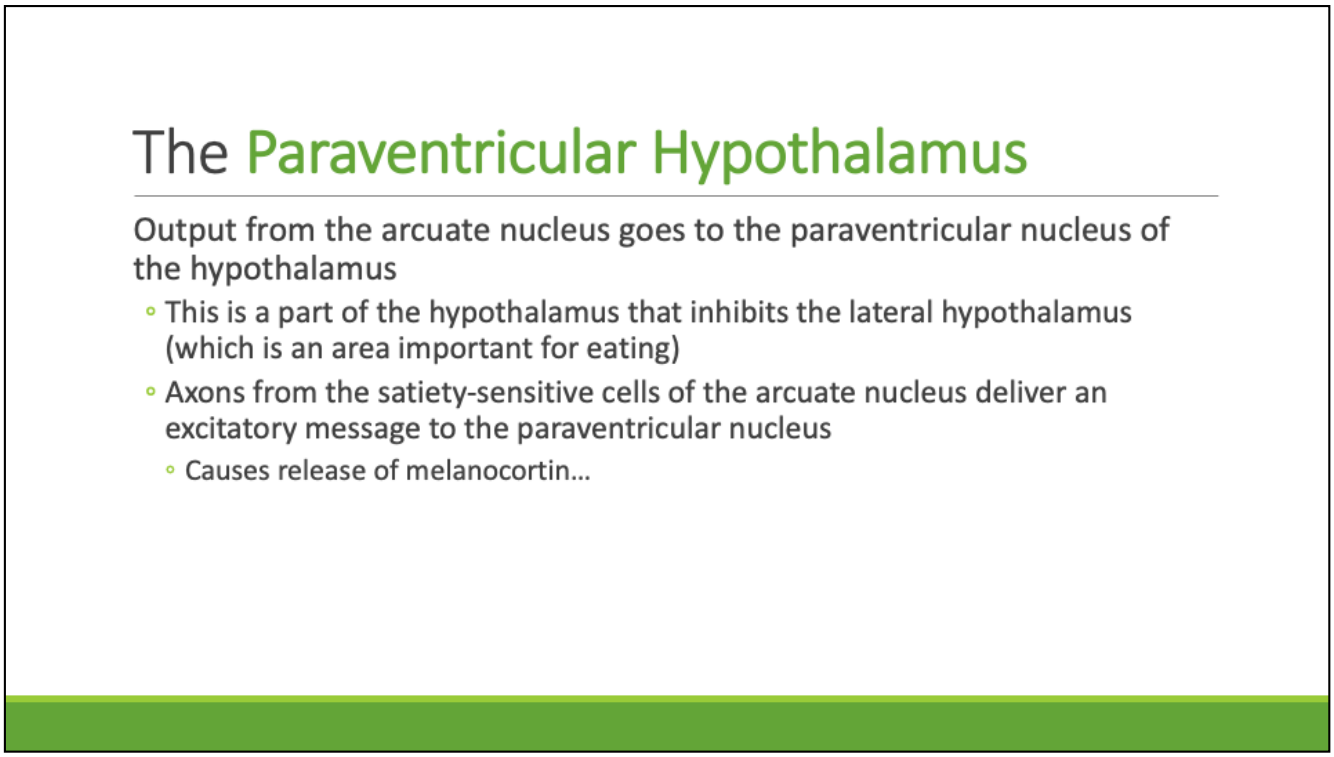
Firstly, hunger/satiety information from all parts of the body connect to one specific area of the brain – the arcuate nucleus – which is located in the hypothalamus (I'm sorry, I couldn't find a good image of this area for some reason).

The Arcuate Nucleus

Input to the satiety-sensitive cells of the arcuate nucleus…

- Signals of both long-term and short-term satiety
- Distention of the intestine triggers neurons to release the neurotransmitter CCK
- Blood glucose stimulates satiety cells in the arcuate nucleus
- Body fat releases leptin

You can read a little more about this structure in the slide above. As you're reading, I'd like you to think about how each component of hunger functions (e.g., CCK, glucose, leptin), and how they're related to the functioning of the arcuate nucleus.



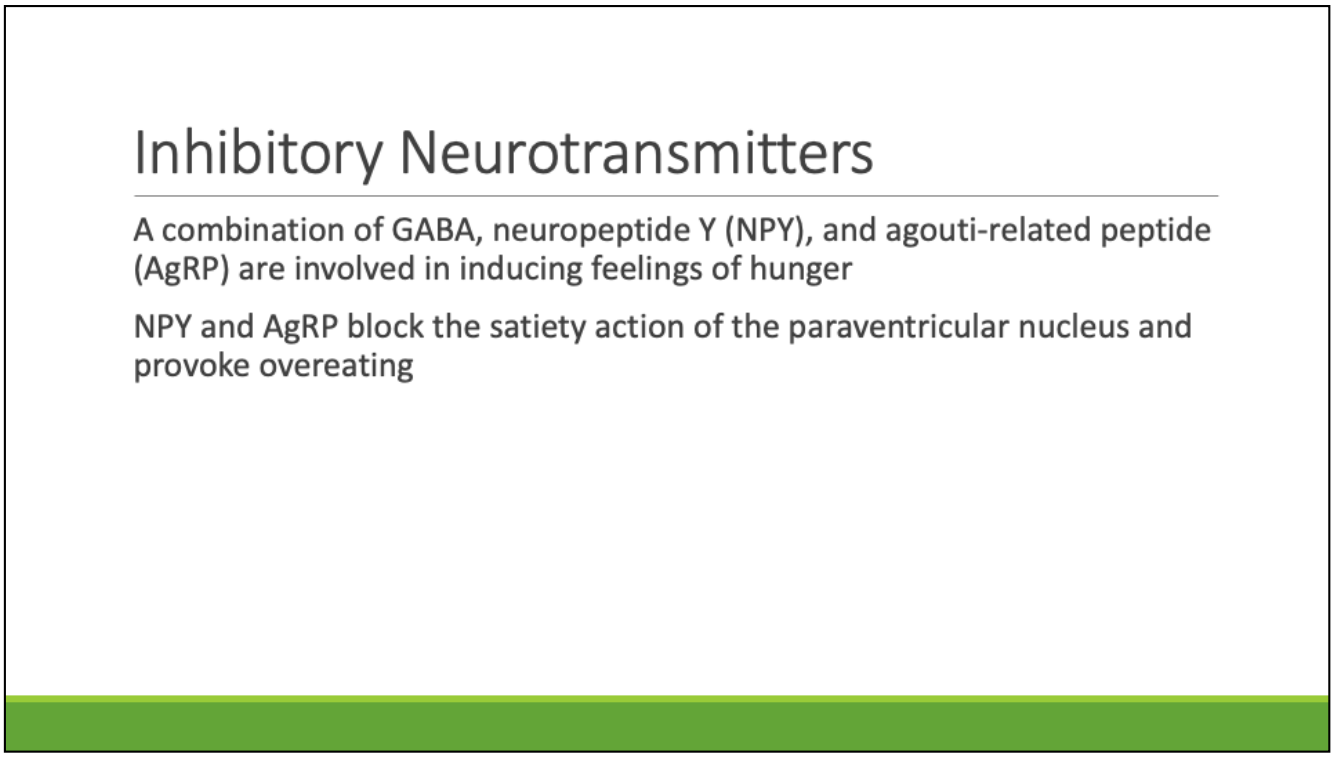
Signals travel from the arcuate nucleus to the paraventricular nucleus, which is also located in the hypothalamus. You can read more about this area above.

Melanocortin

Chemical important in limiting food intake
- Deficiencies of this receptor lead to overeating

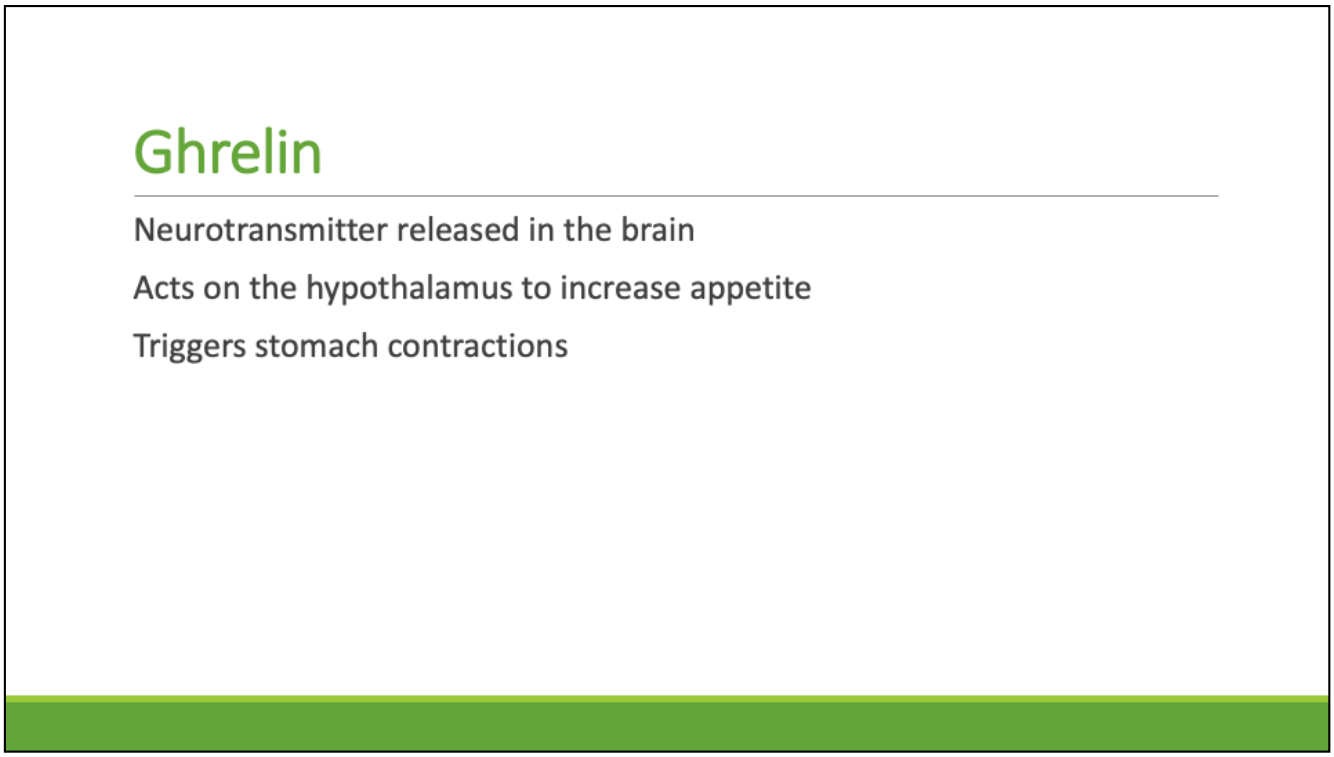
Receives input from the hunger cells of the arcuate nucleus…
- *Excites* the paraventricular nucleus
  - Which, in turn, inhibits the lateral hypothalamus and induces satiety

As mentioned in the previous slide, excitation from the satiety-sensitive area of the arcuate nucleus cause the paraventricular nucleus to release a chemical called melanocortin. This chemical is responsible for promoting feelings of satiety. You can read more about it above.



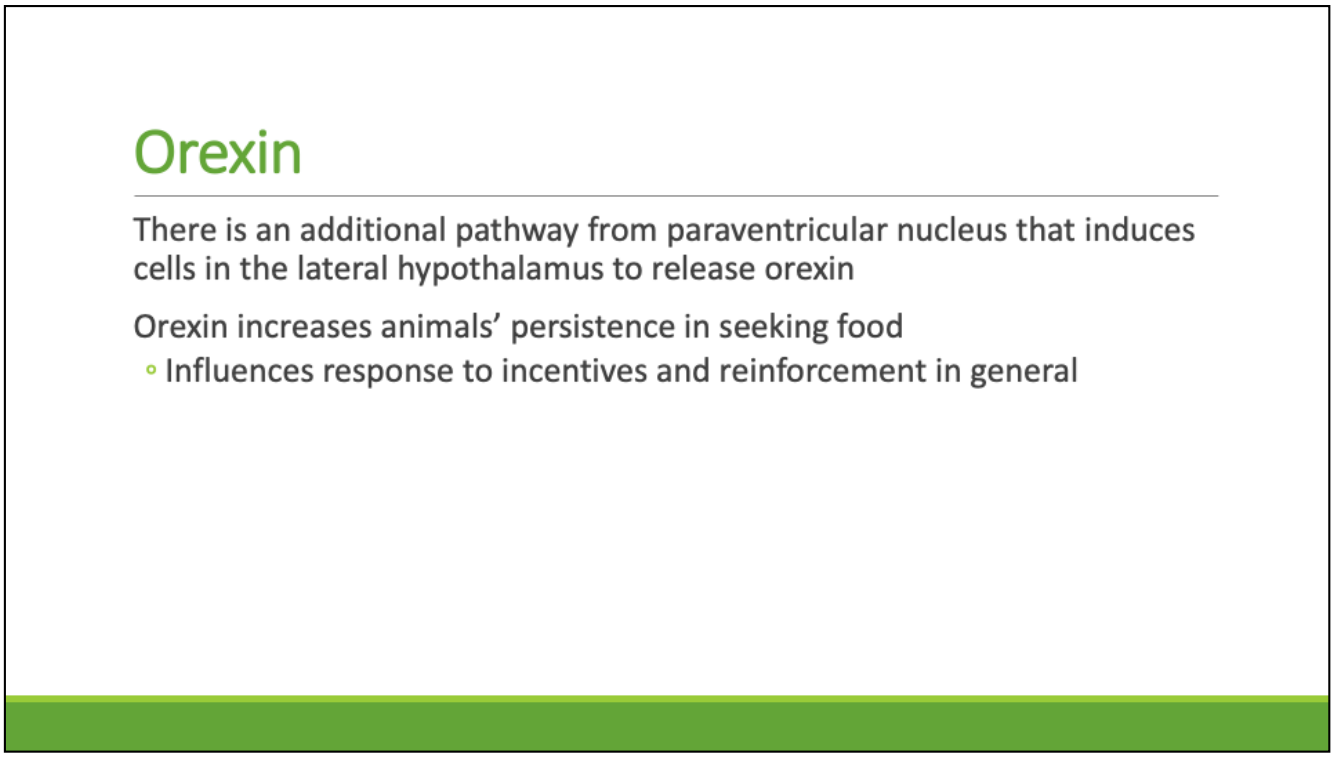
So there are three inhibitory neurotransmitters involved in feelings of hunger and satiety: GABA, neuropeptide Y (NPY for short), and agouti-related peptide (agRP for short). These neurotransmitters *inhibit* the paraventricular nucleus. In the previous slide, I mentioned that excitation of the paraventricular nucleus inhibits the lateral hypothalamus, which creates a feeling of fullness.

On the flipside, inhibition of the paraventricular nucleus prevents an animal from feeling full – that is, it promotes a feeling of hunger



A neurotransmitter known as ghrelin functions to increase hunger. You can read more about it in the slide above.

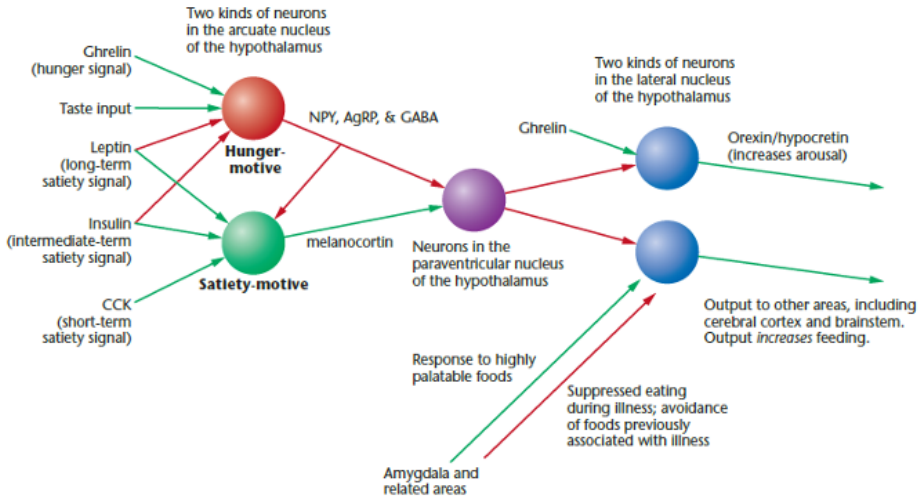
Ghrelin increases appetite both by up-regulating the reward system in response to food, and inhibiting the parts of the vagus nerve that measure stomach distension. It also triggers stomach contractions, which increases the rate of digestion (and specifically, the emptying of the stomach).



Finally, we have orexin (a.k.a. hypocretin), which is a neuropeptide involved in both sleep and hunger.

Signals from the paraventricular pathway trigger the release of orexin in the lateral hypothalamus, which induces a feeling of hunger. You can read (slightly) more about it in the slide above.

Hypothalamic Transmitters of Feeding



Last quarter I made a fantastic joke in class about how this chart would be on the exam. The look of sheer terror on everyone's face… It just doesn't have the same effect in writing :/

In any case, you do NOT have to memorize this chart for this class. However, if you take a few minutes to examine it (I recommend starting with one specific tract [hunger vs. satiety motive] and slowly following it from start to finish), you'll see that it gives an incredibly good explanation of how the hunger and satiety systems work in tandem. Green lines here are excitatory, and red lines are inhibitory.

As an example, hunger signals increase feeding by inhibiting inhibitory messages to the lateral hypothalamus. You can see that if you start at the "hunger-motive," and notice that the inhibitory signals from both leptin and insulin cause the release of inhibitory neurotransmitters (such as GABA), which in turn inhibit the functioning of the paraventricular nucleus. Inhibition of inhibition leads to excitation, and that excitation plus the addition of ghrelin serve to increase appetite. Okay, now it's your turn to try that, but with the "satiety-motive" pathway!

The Lateral Hypothalamus

Feeding-related functions of the lateral hypothalamus…

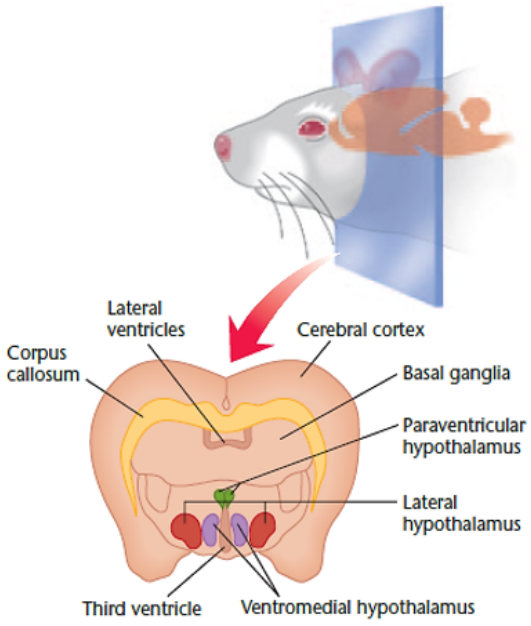
- Controls insulin secretion
- Alters taste responsiveness

Stimulation of the lateral hypothalamus increases the drive to eat

- Damage to this area causes aversion to food

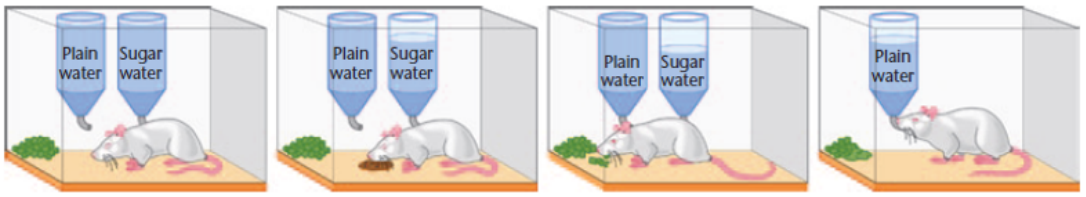
All of these signals eventually end up at the lateral hypothalamus, which triggers the motivational behaviors associated with hunger and satiety. You can read a brief summary of this structure above, and we'll talk about it in more detail over the next few slides.

The Lateral, Ventromedial, and Paraventricular Hypothalamus



Before we get into it, this is a coronal view of a rat brain that shows the location of the lateral, ventromedial (which we haven't discussed much), and paraventricular sections of the hypothalamus. The human brain is structured similarly, at least in terms of these areas, and so this is a helpful comparison to make. Again, you don't need to memorize these locations – this is just here to give you a point of reference when you're thinking about these areas.

Recovery after damage to the lateral hypothalamus in rats



Stage 1. *Aphagia and adipsia.* Rat refuses all food and drink; must be force-fed to keep it alive.

Stage 2. *Anorexia.* Rat eats a small amount of palatable foods and drinks sweetened water. It still does not eat enough to stay alive.

Stage 3. *Adipsia.* The rat eats enough to stay alive, though at a lower-than-normal body weight. It still refuses plain water.

Stage 4. *Near-recovery.* The rat eats enough to stay alive, though at a lower-than-normal body weight. It drinks plain water, but only at meal-times to wash down its food. Under slightly stressful conditions, such as in a cold room, the rat will return to an earlier stage of refusing food and water.

But let's talk a little more about the functions of the lateral hypothalamus. If you damage the lateral hypothalamus in rats, they will completely refuse food and water at first. If you force feed them for a period of time, they'll eventually – and very slowly – regain their normal appetites. However, their appetites will never return to normal – they'll eat just enough to stay alive, and only drink during meals to wash down food. Also, if you expose them to stressful conditions, they'll revert back to refusing all food and water.

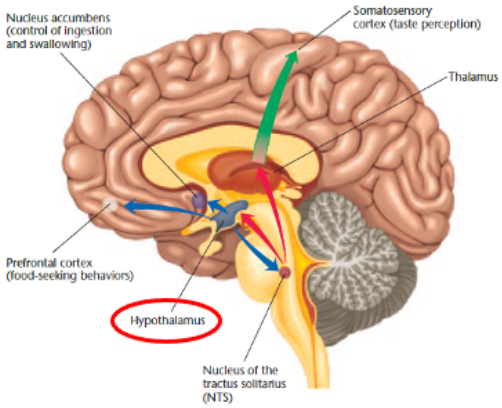
The take-home message here is that changes to this area can be pretty devastating, and even though recover occurs to some degree, individuals with a damaged lateral hypothalamus never make a full recovery.

The Lateral Hypothalamus and Axons

Many axons containing dopamine pass through the lateral hypothalamus

Axon functions…

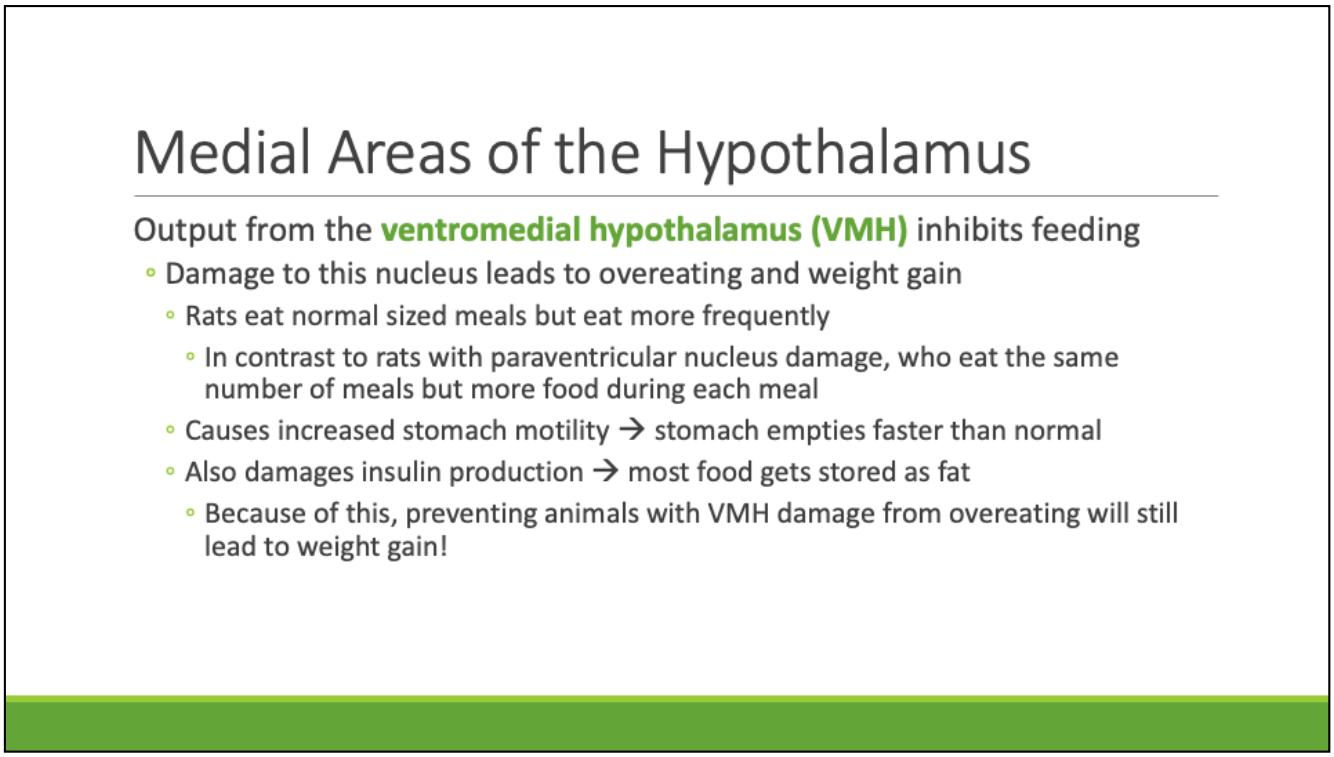
- Affect the taste sensation and salivation response to tastes (via signals to the nucleus of the tractus soltarius (NTS)
- Cause cortical cells to increase response to taste, smell, or sight of food (via signals to, e.g., the prefrontal and somatosensory cortices)
- Increase pituitary gland's hormone secretion, which increases insulin secretion
- Control digestive secretions (via signals to the spinal cord)



The pathways of the lateral hypothalamus are dopaminergic, meaning the axons that comprise these pathways are primarily involved in the transmission of dopamine.

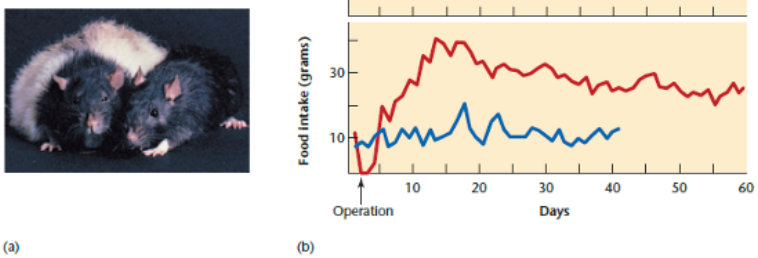
These axons fire onto a number of different areas and have a number of different functions, all of which you can read about in the slide above.

The diagram above shows a number of the different pathways we've been discussing over the past few slides. You can see that this area plays a fairly large role in a lot of the different processes in charge of hunger and satiety! It can alter motivational states, modulate insulin release, even control digestive secretions.



Finally, we have the ventromedial hypothalamus (VMH), which also plays a role in eating behaviors. Specifically, this area seems to respond to satiety, and stops feeding behavior as a response. If you damage this area, it will lead to overeating and weight gain. You can read more about consequences of VMH damage in the slide above.

Effects of Damage to the Ventromedial Hypothalamus



(a)

(b)

This first image here shows a comparison between two rats: the one on the left has a damaged VMH, and the one on the right does not.

The graph shows the difference in eating behavior between rats with an intact vs. damaged VMH. Shortly after damaging the VMH, rats will begin eating *way* more than their intact counterparts – you can see that by looking at the red line (which is the damaged rat) and comparing it to the blue line (which is the rat with the intact VMH).

Eating Disorders

Availability of tasty, high calorie foods makes animals (and people) obese, and they find other rewards less rewarding

Psychological distress does not appear to cause weight gain

- Weak link between depression and weight gain, but not significant enough to be a primary factor

A high-fat diet before birth can result in the offspring being born with a larger than average lateral hypothalamus

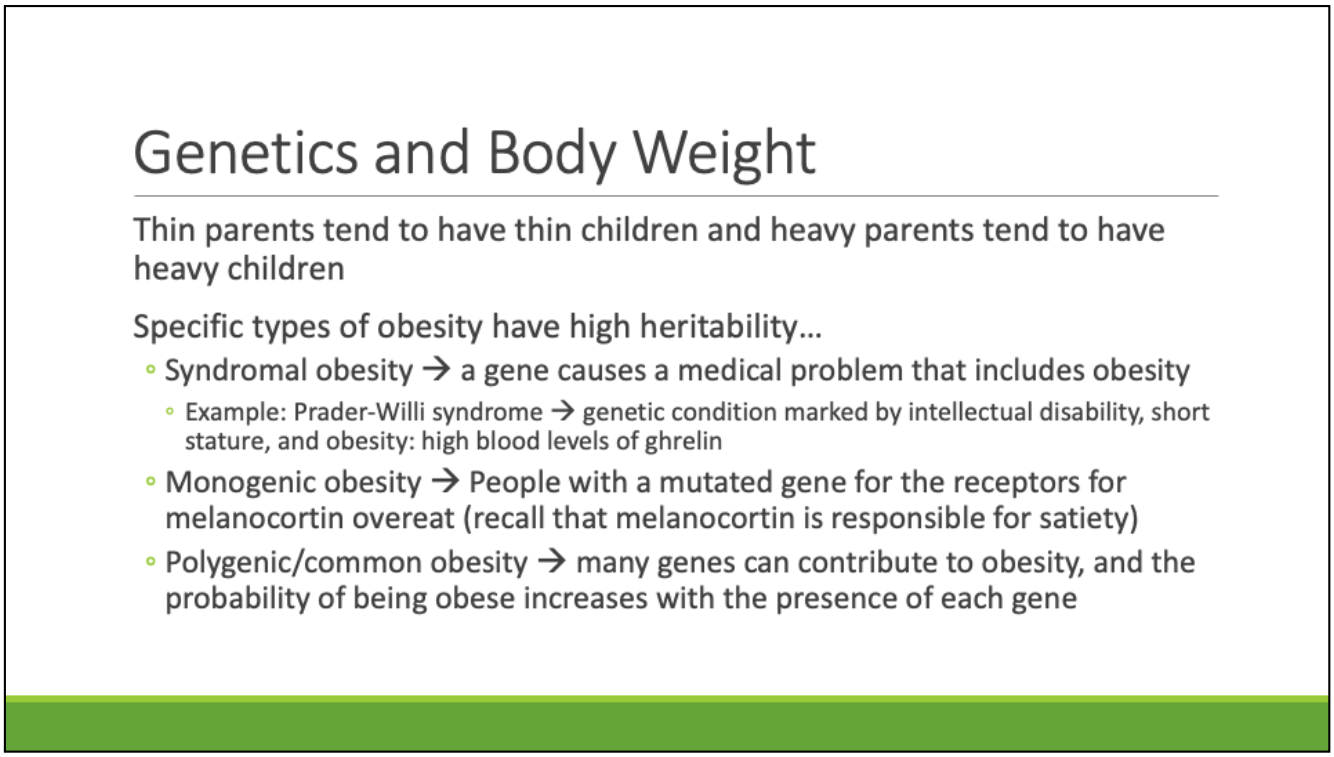
- Produces more orexin and other neurotransmitters that lead to increased eating behaviors

Other disorders not discussed here (which you should know for the exam):

- **Bulimia nervosa**
- **Anorexia nervosa**

Let's finish up by discussing a few cases of non-typical eating and satiety behavior. I say that these instances are non-typical because they are less common compared to what we consider "average" food consumption behaviors (although as a caveat this concept of "average" can be subject to a number of different factors that cause it to vary over time and across cultures). These behaviors may also be harmful to individuals that exhibit them.

You can read more about these different behaviors in the slide above.



There is some indication that body weight is determined, at least in part, by genetics. As a general example, thin parents tend to have thin children, and heavier parents tend to have heavier children.

More specifically, it appears that specific types of obesity have high heritability – meaning that more of their variance can be attributed to genes vs. environmental factors. You can read more about these cases above.

Questions for your discussion groups…

1. How do insulin, glucose, and glucagon work together in the cycle of hunger and satiety?
2. What are ghrelin, orexin, and melanocortin, and how do they each contribute to feelings of hunger/satiety?

Okay, that does it for this week! I know I've been saying this for the last three weeks, but I can actually hold full conversations with people now, so by next week I will have my voice back enough to give our last lecture. Good luck this week, and I hope to see you in the lecture chat!