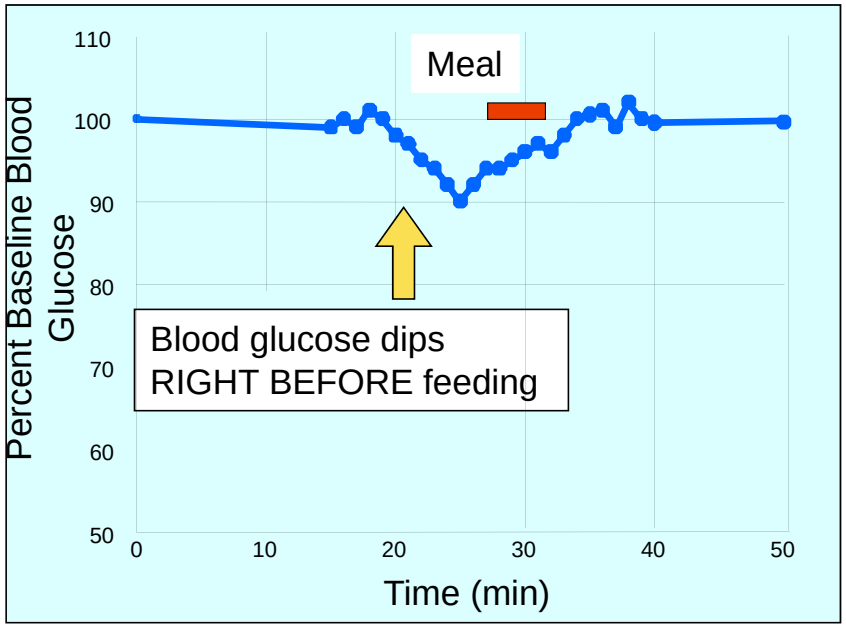
Homeostasis, Feeding (Ch.13) II

- Multiple factors that influence feeding behaviour
  - Factors that influence feeding- blood glucose fluctuations
  - Factors that determine satiety
- Neural mechanisms of feeding
  - Liver and gut hormonal signals
  - Ventromedial and Lateral hypothalamus
  - Arcuate Nucleus of Hypothalamus
    - Short-term interactions between body-based satiety signals and brain
  - Bypassing body signals (conditioned feeding)
  - Serotonin (5-HT) suppression of feeding

Changes in blood glucose around feeding time

- ***Study***: provide rats w/unlimited food- monitor glucose levels
- Blood glucose levels remain constant through day *except…*
- Glucose levels drop ~10% before feeding is initiated
- **However,** it is unlikely that drop in glucose is directly responsible for feeding because:
- **If food taken away (no meal)** = glucose levels return to previous homeostatic levels in about 10-15 min.



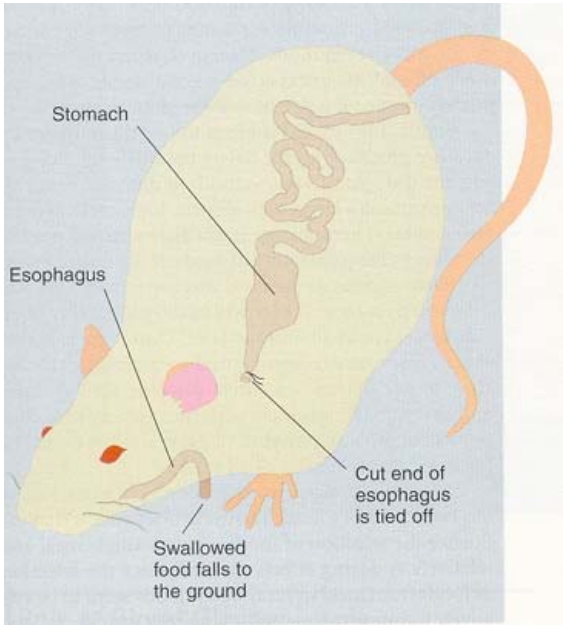
- Decline may be related to INTENTION to eat (not other way around). Drop in blood glucose is preceded by increased insulin, so drop may have been actively produced (not a decline in "energy reserves").

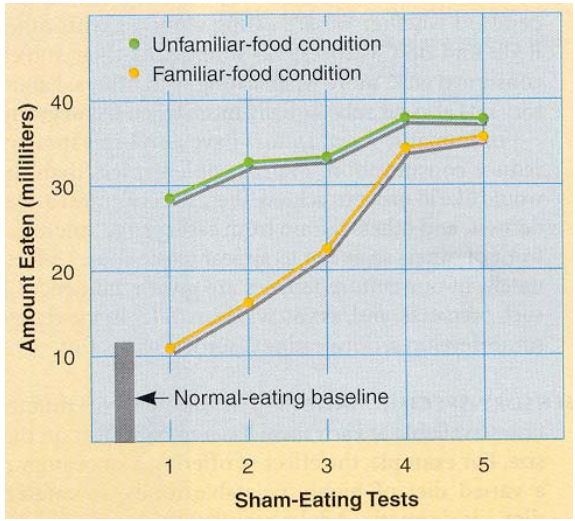
- Changes in glucose levels may contribute to feelings of hunger, but does not seem to be the main controller of eating behavior

Factors that influence satiety (I)

- **Previous experience about nutritive value of certain foods influences satiety**

- **Sham eating experiment**: Food is chewed, swallowed, passes out of the body (not digested). Rats given either normal lab chow (which they are used to) or novel food
- With normal lab chow, rats start off eating same amount as before surgery. Give rats a **novel** food- they eat more.





Not until 4th meal that rats are eating 3 times as much as normal. Even then they stop feeding.

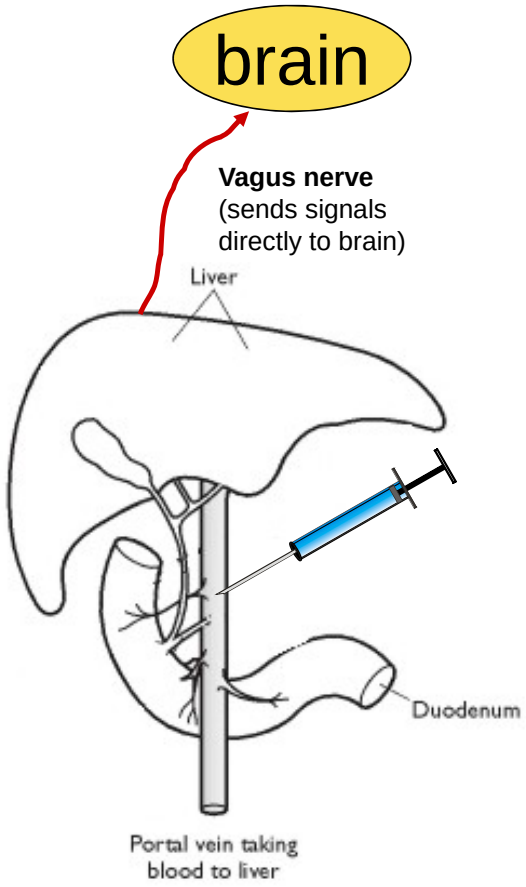
Factors that influence satiety (II)

- **Social Influences:** Humans and animals eat more in groups vs alone
  - ***Study*:** When two individuals eat together, they tend to take "bites" together, eat similar amounts of food

- **Sensory Specific Satiety**: Humans and animals take in more calories if they are given varied (cafeteria, buffet) diet
  - Satiety can be taste specific: new taste = more consumption
  - Encourages consumption of varied diets and to take advantage when different foods are abundant
  - ***Study***: humans asked to rate palatability of 8 foods, then given one of foods for meal
  - When asked again to rate same 8 foods, one they just ate got lower rating: when given new meal right after, they ate more.

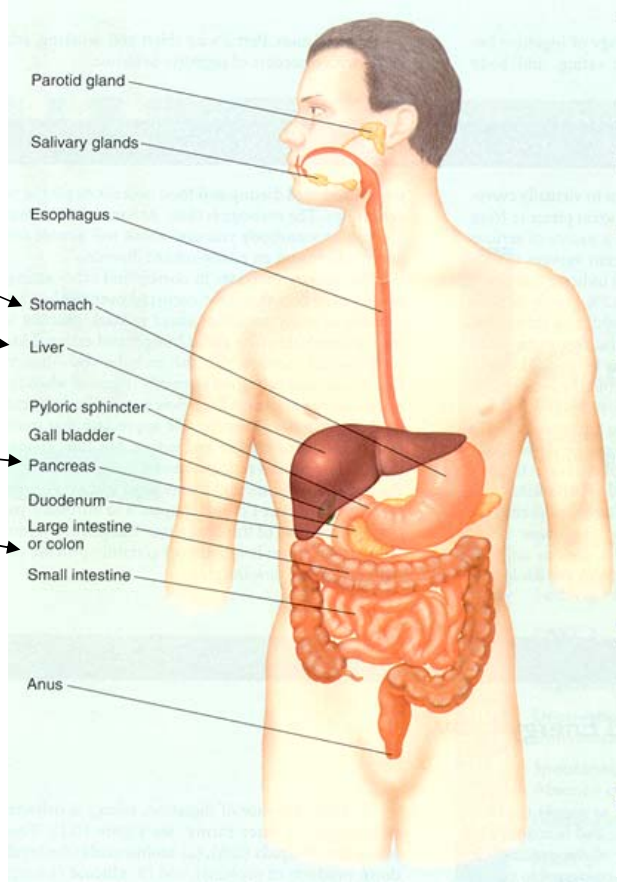
Physiology of Hunger and Satiety

- Liver can signal brain about what's in the bloodstream via vagus nerve
  - Liver receives blood from small intestine; has *detectors* for glucose and fatty acids inside some cells
- **Experiment**: inject chemicals that "trick" liver to act as if glucose/fat levels are low
  - **2-deoxyglucose (2-DG)** = competes with glucose for absorption, but *doesn't activate glucose detectors*
  - **Methyl palmoxirate** = disrupts metabolism of fatty acids
- Inject these drugs into vein from intestine → liver = immediate increase in feeding
- Cut vagus nerve = abolish effect of drug injection
- **Note**: brain also has receptors for glucose (but not fats) in a number of regions.
  - Infusing 2-DG in certain brain regions also stimulates feeding



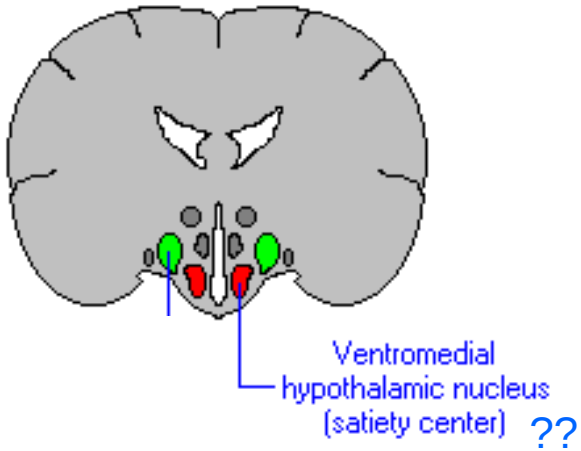
Satiety/Hunger Signals: Body to Brain

- Body uses multiple hormones to signal brain to start/stop eating
- Food in gut, glucose in blood can initiate ***signals that suppress hunger*** before food is fully digested
  - **From Stomach**: CCK, bombesin, somatostatin
  - **From Liver**: detects changes in blood glucose, direct input to brain via vagus nerve (non-hormonal)
  - **From Pancreas**: Insulin
  - **From Intestines**: PYY_{3-36} & GLP-1
  - **From Fat Cells:** Leptin, gives continuous feedback on body's energy stores
    - Removal of fat gets rid of this satiety signal, increases hunger
- Other peptides can stimulate feeding
  - **From Stomach:** Ghrelin, levels remain high during fasting, drop during meal (short term)



Neural Basis of Hunger and Satiety (I)

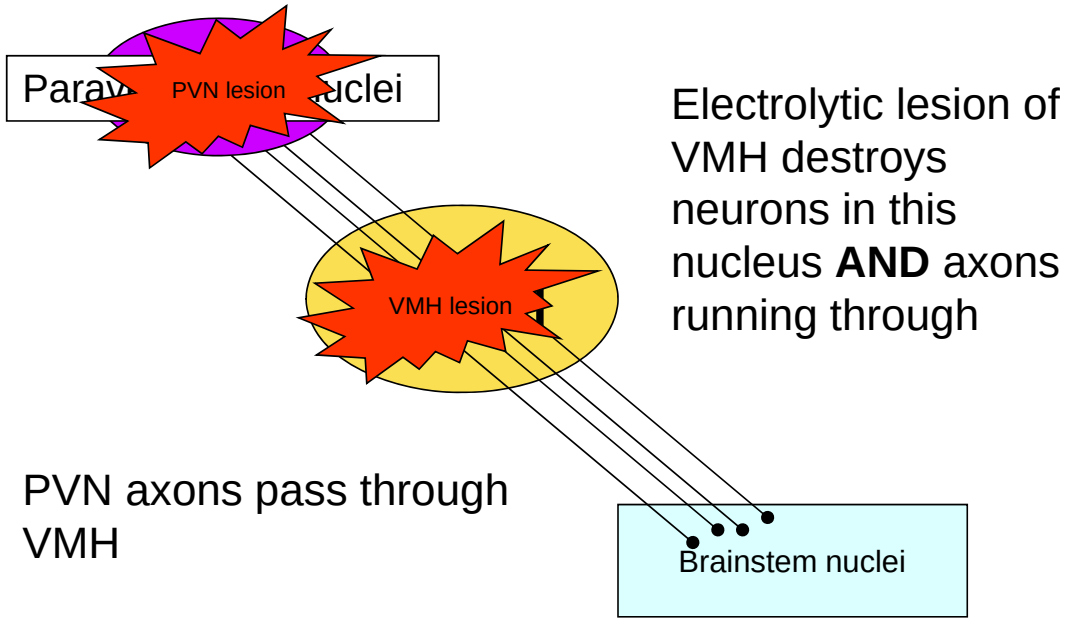
- **Ventromedial Hypothalamus:** Satiety center?
  - Lesion this nucleus, animals become obese
  - Starts with massive consumption that achieves new weight **(dynamic phase)** then maintenance of that weight **(static phase)**
  - **Interpretation issues:** Animals reach a new target weight, but do eventually stop eating in a session
  - Rats become "*finicky*" eaters: give rats less palatable food, VMH lesioned rats show minimal weight gain



  - **Reinterpretation**: VMH regulates energy metabolism, not eating.
  - VMH lesions increase insulin levels (which increases *lipogenesis* (fat formation) and decreases breakdown of body fat into usable forms)

VMH lesions

–Neurons in VMH may not be what causes effects. These lesions also destroy axons projecting from the ***paraventricular nuclei*** of the hypothalamus. Lesions of these fibers alone also produce hyperphagia and obesity.



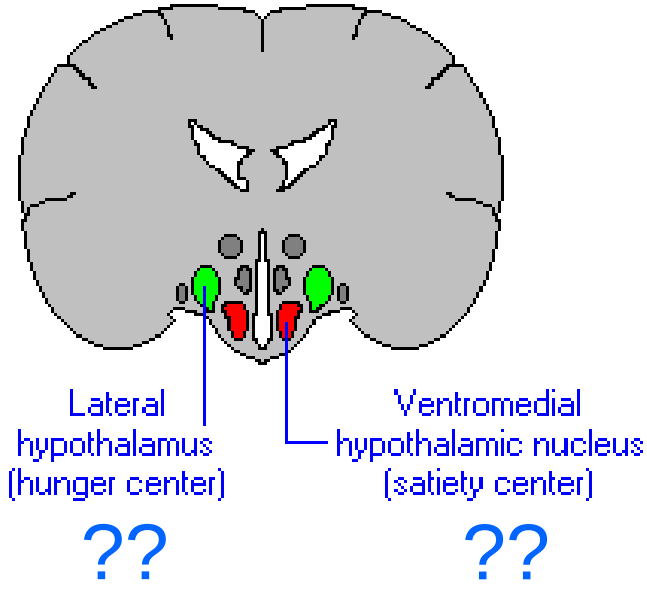
Electrolytic lesion of VMH destroys neurons in this nucleus **AND** axons running through

PVN axons pass through VMH

•Destroy PVN or axons = same obesity and hyperphagia as VMH lesions

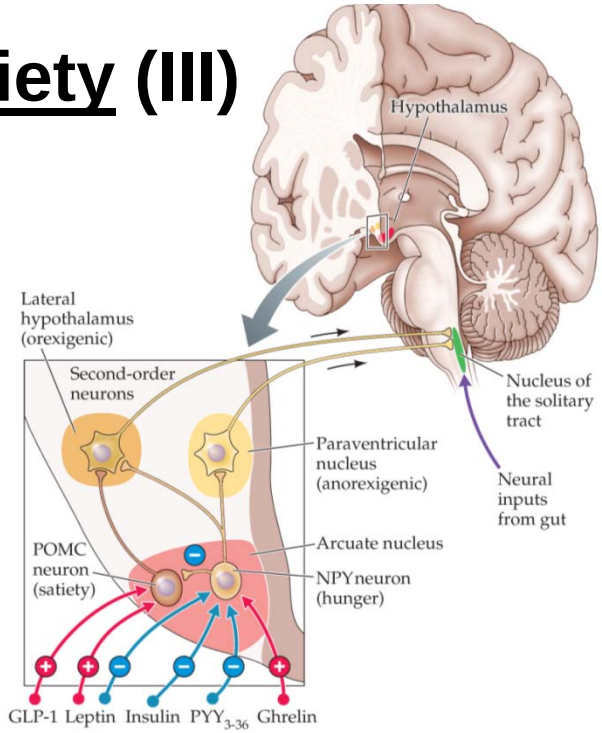
Neural Basis of Hunger and Satiety (II)

- **Lateral Hypothalamus:** Hunger center?
  - Lesion caused rats to stop eating (**aphagia**)
  - **Interpretation issues:** force feed rats for a week, they eventually start eating again
  - **Reinterpretation:** LH lesions cause wide range of sensory and motor disturbances, including decreased appetite. Animals have problems with eating, but not lack of hunger.



- **Control of hunger and satiety** is distributed across many brain regions
  - Other hypothalamic subregions, as well as amygdala, frontal cortex are also involved

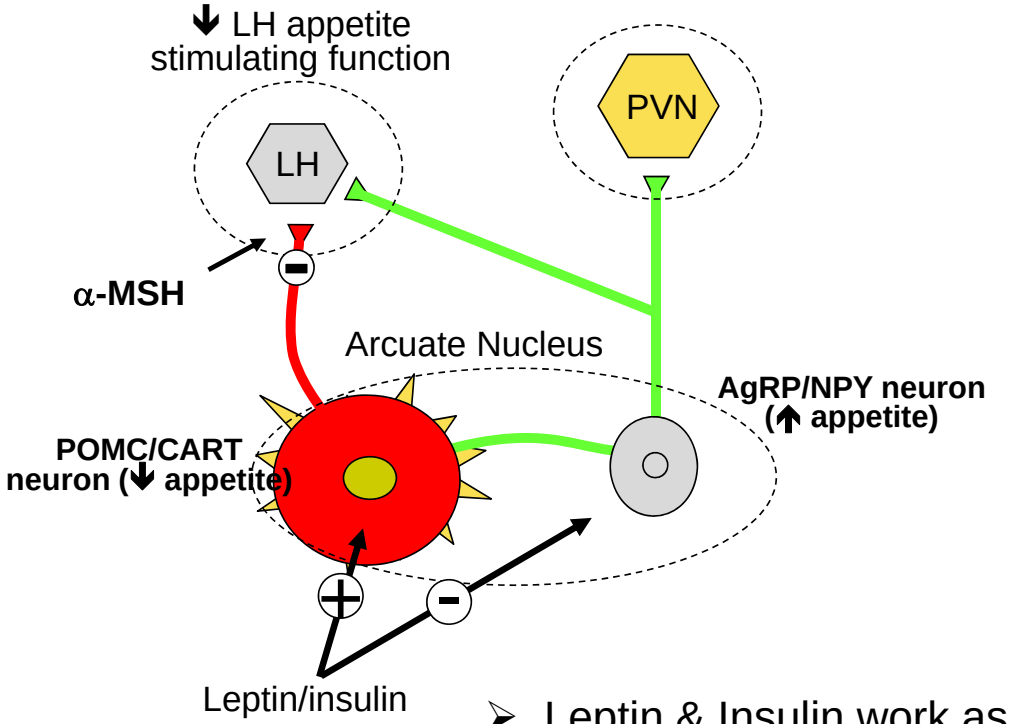
Neural Basis of Hunger and Satiety (III)

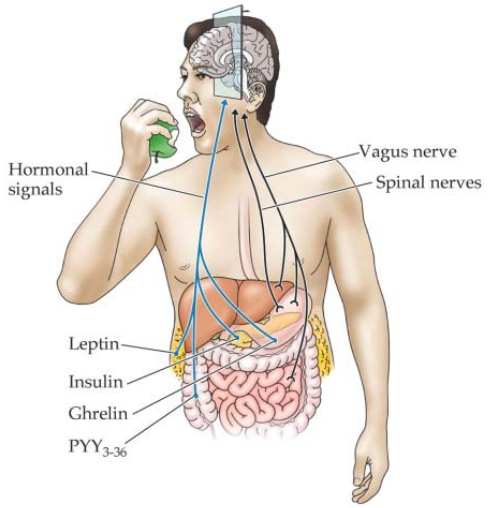


- **Arcuate Nucleus of Hypothalamus:** First-pass appetite control center
  - 5 main Satiety/Hunger hormone signals from body interact with this nucleus to regulate feeding
  - **Pancreas**: Insulin (↓ feeding) **Fat Cells:** Leptin (↓ feeding)
  - **Intestines**: GLP1 & PYY_{3-36} (↓ feeding) **Stomach:** Ghrelin (↑ feeding)
  - These activate different types of neurons in arcurate nucleus, (defined by transmitters they use or proteins they express)
- **Neuropeptide Y (NPY) & agouti-related peptide (AgRP)**
  - Activation of these cells ↑ appetite
- **Pro-opiomelanocortin (POMC) & Cocaine/Amphetamine regulated transcript (CART)**
  - Activation of these cells ↓ appetite

Arcuate Neural Circuitry and Appetite (I)

(Long-term appetite control)

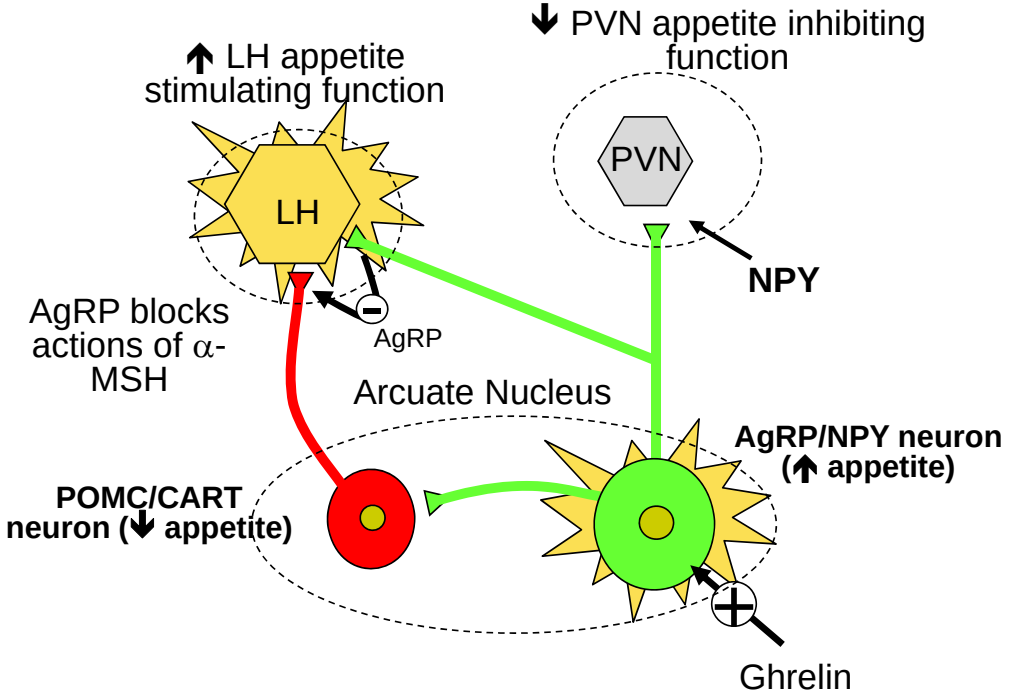


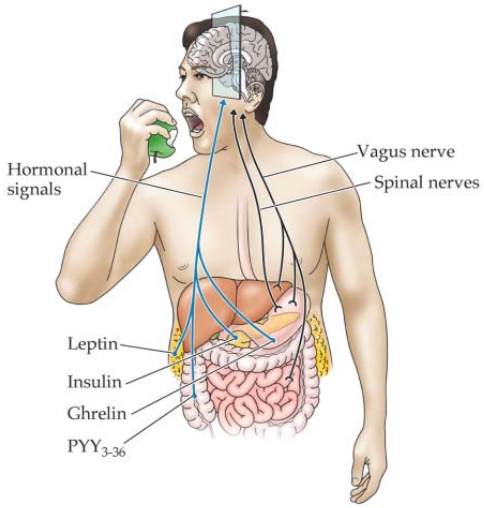


- Leptin & Insulin work as long term modulators of appetite
- •Activate POMC/CART neurons ***and*** inhibit AgRP/NPY neurons
- •POMC/CART neurons inhibit lateral hypothalamus (LH) using the transmitter **α-melanocyte stimulating hormone**

Arcuate Neural Circuitry and Appetite (II)

(Short term appetite **increase** during fasting)

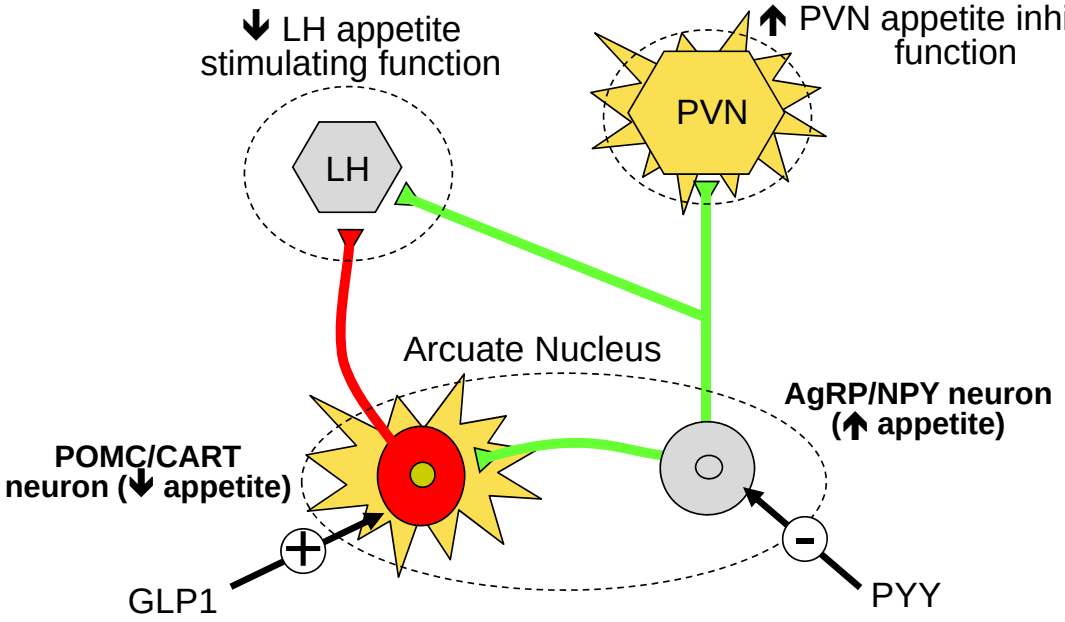


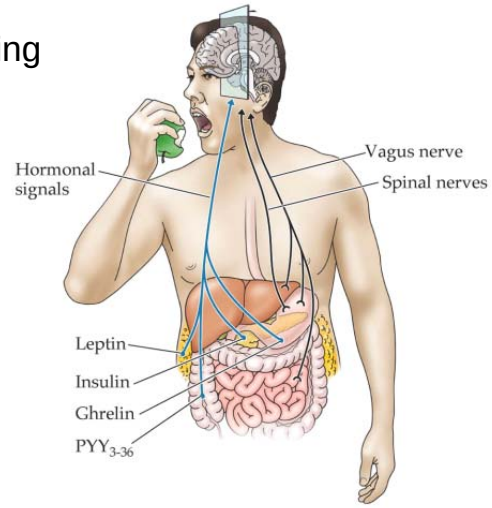


- Ghrelin released by stomach when empty, stimulates AgRP/NPY neurons that do 2 things:
  - Inhibits PVN cells using the transmitter NPY
  - Release AgRP in LH, and this blocks α-MSH inhibition (acts as an antagonist on these receptors), leading to increased LH activity

Arcuate Neural Circuitry and Appetite (III)

(Short term appetite **decrease** after meal)



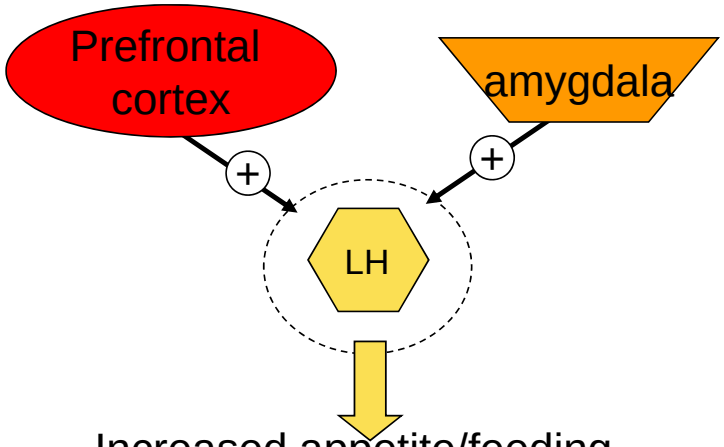


- PYY & GLP1 released from intestines in response to meal
  - **PYY** inhibits AgRP/NPY neurons, which disinhibits (i.e.; increases) PVN activity
  - **GLP 1** stimulates POMC/CART neurons, which inhibits LH activity

Bypassing the Hypothalamic Feeding Circuit

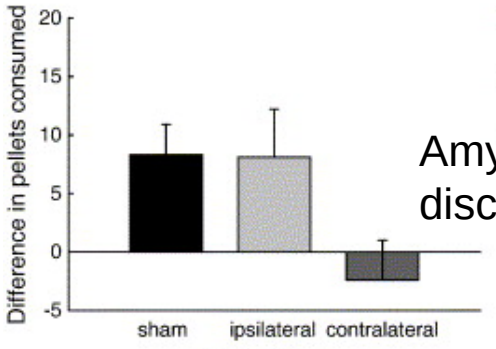
- Arcuate nucleus circuitry can be bypassed by food-associated cues
- Rats given food + cue that predicts foods delivery
- Present cues in sated rats, they eat more (*Pavlovian conditioned feeding*), **but…**
- Lesions to **prefrontal cortex or amygdala, or disconnection** of the **amygdala-LH pathway abolishes *conditioned* increases in feeding**
- **NOTE: NORMAL** feeding patterns unaffected by these lesions.
- These lesions only disrupt *cue-induced feeding*

These regions are activated by cues associated with feeding



Increased appetite/feeding

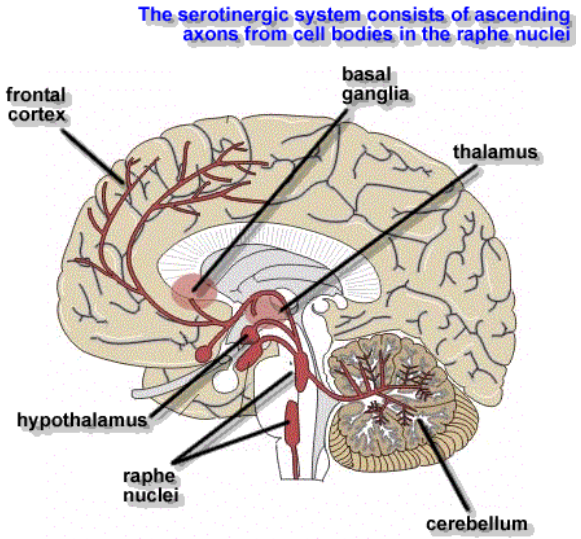
Feeding induced by cue



Amygdala-LH disconnection

Neurochemistry of Hunger and Satiety

- **Serotonin (5-HT):** a major brain satiety signal
- 5-HT agonists or releasers (e.g. Prozac) in humans and animals can:



🡻 feeding, even with cafeteria diets

🡻 amount of food consumed per meal but ***not*** number of meals per day

-Increased 5-HT activity shifts food preference ***away*** from fatty foods
-5-HT acts as short term satiety signals associated with meal consumption

Brain regions: 5-HT **inhibits release of NPY in the PVN** of hypothalamus, which then disinhibits PVN neurons to promote satiety