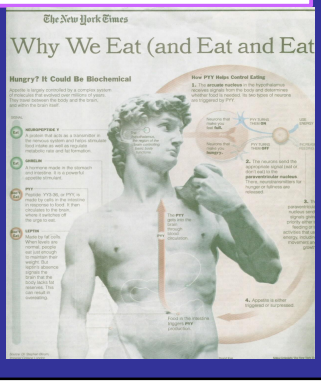
Biology 402 Lecture 10

- Grades posted ~ average 76%
- Anyone with less than 60% MUST see me.
- Lab exam will be scheduled for next week. This week both groups will do tutorials
- Appetite regulation

Appetite Regulation

- Science Times 11/ 26/ 2002.
- Nature Aug 2002. 418:650.
- Pubmed more than 60000 papers since 1980. ? Still controversial !!
- Energy balance
- Appetite, satiation and satiety
- Neural regulation
- Hormonal regulation

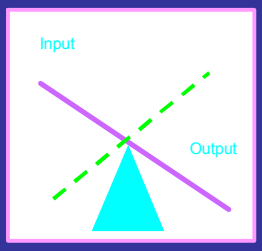


Why regulate food intake?

"It is worth keeping in mind that hunger is a biologically useful sensation. It is a nagging irritating feeling that prompts thoughts of food and reminds us that the body needs energy".

- Biological drive to eat served us well when we were hunter/gathers uncertain when our next meal would be but in modern times when our next meal is waiting in the refrigerator or at the corner café, out of kilter.
- Obesity (>60% US population overweight) pathological consequences such as diabetes, cardiovascular problems, cancers.
- Inanition similarly is life threatening (muscular, respiratory, CV, cellular underfunction e.g. anorexia)

Energy Balance Equation most animals exquisite regulation



- Storage / loss
  Obesity /
  undernourishment

Regulation of Food Intake

Ingestion of food is a complex process that integrates

a) sensory information related to sight, smell, & taste of food,
b) previous ingestion experience,
c) satiety signals elicited by ingestion,
d) hormonal signals related to energy balance, &
e) circadian rhythms by SCN

Information about body energy & nutritional status (from gut, liver, & fat stores) is continuously transmitted to brain by

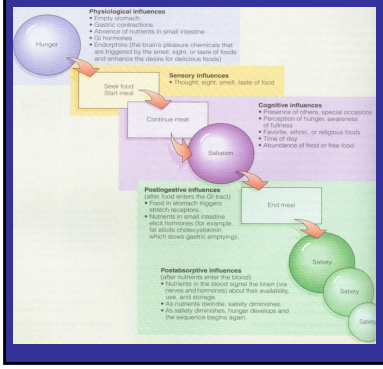
1) the afferent autonomic neurons,
2) changes in conc of circulating nutrients and hormones
3) gastrointestinal and central neuro-endocrine mediators.

Many back-ups, modulators and mediators. Strong links between temp reg., sleep, repro. hormones and appetite reg.

Regulation of Food Intake.
Definitions of key terms

- Hunger
  - Craving for food
- Appetite
  - Drive to eat
- Satiation
  - Cessation of eating during a meal
- Satiety
  - Between meal fullness, stops the drive to eat

Appetite, satiation and satiety



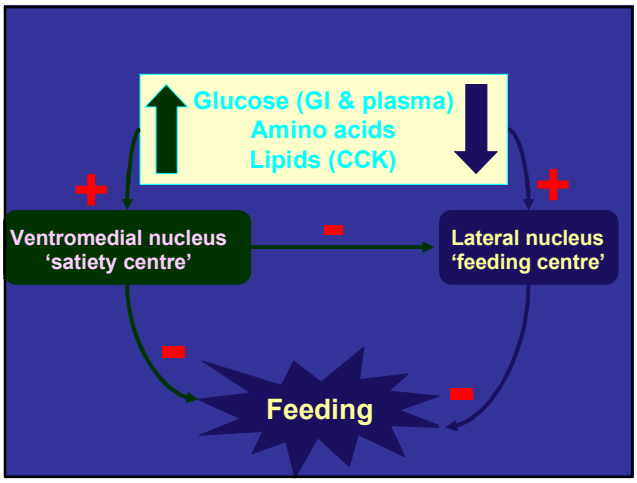
- Appetite: desire to eat. Seek food.
- Start meal
- Continue meal until full
- Satiation: stop eating
- Satiety: stay full, no desire to eat. As nutrients dwindle satiety dwindles, hunger develops.

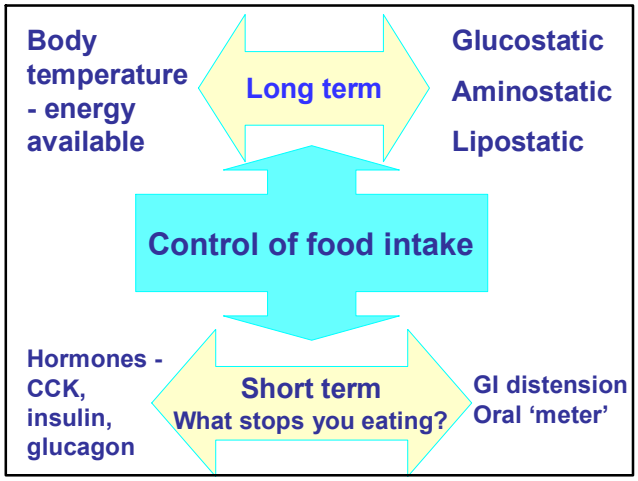
Regions of the brain regulating drive to eat, stop eating and between meal fullness.

- Appetite
  - Arcuate nucleus
- Satiation
  - Lateral hypothalamic area (LHA)
    - Electrical stimulation hyperphagia
    - Destruction aphagia
- Satiety
  - Ventromedial hypothalamic nucleus (VMN)
    - Stimulation refusal to eat,
    - Destruction uncontrolled eating

Appetite and satiety regulators

- Many substances influence satiety and appetite. Back up systems
- All modulate rather than are key regulators.
- Hormones e.g. Insulin, leptin
- Metabolites e.g. Glucose FFA
- Cognitive e.g. See-food diet
- Stretch e.g. Gastric stretch





External cues that contribute to appetite stimulation

Environment
- Place of eating
- Availability of food (fridge)
- Time of day
- Ambient conditions

Social
- No. of people
- Occasion

Opportunity
- Coffee break
- In between lectures

Convenience
- Habit
  e.g. Subway coffee wagon

Internal cues that contribute to appetite regulation

Psychological

- Cognitive
- Conscious
- Learned behavior
- Conditioning
- Stress levels

Physiological

- **Metabolic**
  Glucose and FFA
- **Hormonal**
  Insulin, Leptin, Glucocagon, NPY, a-MSH,Orexin, CCK, Ghrelin, PYY, Estrogen/Prog
- **Mechanical**
  Degree of gastric fullness and gastric stretch. Meal frequency

Hormones that increase the desire to eat

»NPY
»Orexin
»Galanin

These decrease sympathetic activity work through NPY .

Hormones that decrease the desire to eat

- PYY
- CCK
- Serotonin
- Alpha-MSH
- Insulin
- CRH
- Leptin
- B-adrenergic receptor activity of SNS: ephedrine, caffeine, glucose
- Leptin feedback from adipocytes
- Work primarily by inhibiting NPY and stimulating melanocortin pathway.

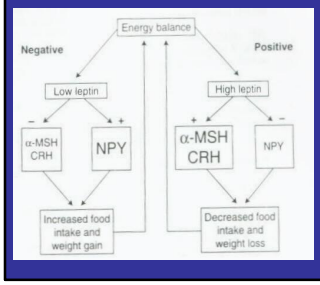
Monoaminergic neurotransmitters regulate food intake

- Dopamine required to initiate feeding.
- Nb in meal frequency.
- Serotonin promotes satiation, inhibits further food intake and is stimulated by carb ingestion.
- Appears that most of the neural input and hormones regulating food intake, meal size and frequency act through monaminergic neurotransmitters dopamine and serotonin in the Ventromedial nucleus (VMN) and LHA.

Arcuate nucleus

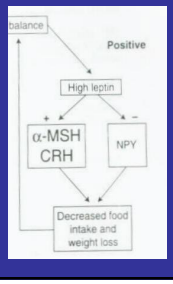
- Neuron dense region with neurons that produce NPY, opioids, B-endorphins, & a-MSH.This region sends signals to the lateral hypothalamic area (LHA) and ventromedial nucleus (VMN).
- LHA controls short term fullness
- VMN long term satiety

Leptin - decreases food intake and increases metabolic expenditure



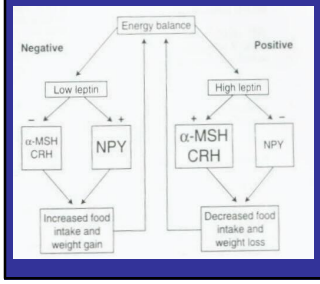
- **Leptin conc dep on. amt of body fat.**
- **High levels of Leptin increase release of POMC from neurons in arcuate nucleus.**
- **POMC cleaves into ACTH, aMSH, B endorphins**
- **A-MSH binds to MC4 receptors-**
  - **Dec food intake**
  - **Inc lipid oxidation**
  - **Inc metabolic rate**
  - **Inc CRH release which directly dec food intake.**

Inc Leptin -



- Increase POMC & cocaine/amphetamine regulated transcript (CART) acts on paraventricular hypoth. nucleus (satiety) and lateral hypo. nucleus (hunger).
- Acts on hypothalamic hormones reg. MR, repro, growth. Also influences feeding behavior and sympathetic nerve fn.

Low Leptin - increases food intake and decreases metabolic expenditure



- Stimulate NPY.
- Inc food intake
- Dec energy expenditure
- Weight gain.

Melanin concentrating hormone

- MCH increases food seeking behavior
- Antagonizes alpha MSH.
- Only knockout gene that truly induces anorexia and lean mass

Gut hormone PYY3-36 inhibits food intake

- Nature Aug 2002.
- Appears to signal meal ingestion to the arcuate nucleus.
- Produced in the gut in direct proportion to the amount of calories ingested.
- Binds to receptor on NPY, inhibiting NPY neuron activity and decreasing food intake. Inc POMC neuron activity
- In humans IV injection of PYY dec food intake by>33% over a 24h period.

Ghrelin inc appetite and weight gain

- Produced in stomach, intestine and placenta.
- Inc GH, inc food intake
- Activates NPY.
- Dec when have stomach reduction surgery and may account for more permanent weight loss via those drastic measures.

Insulin decreases appetite

- Insulin circulates in blood at concentrations proportionate to body-fat mass.
- Decrease appetite by inhibiting NPY neurons while stimulating melanocortin-producing neurons in the arcuate-nucleus
- Obese show insulin resistance.

Match fuel intake to fuel oxidation

- If high carb meal seratonin produces satiety.
- Enterostatin selectively decreases fat intake.

Cholecystekinin (CCK)

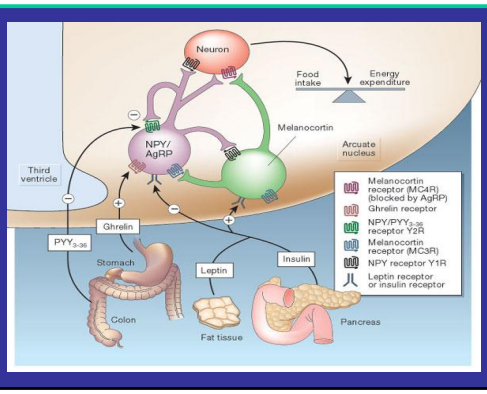
- Brain /gut peptide inhibits food intake acts on vagus nerve and pyloric sphincter.
- Stimulates pancreatic secretion, gall bladder emptying, intestinal motility, inhibits gastric emptying
- Controls meal size.
- Regulates conditioned taste aversions.
- Mediates actions of estrogen, insulin and leptin on long term food intake.

Orexin/hypocretin

- Sleep important in appetite regulation and energy balance
- Total sleep deprivation leads to hyperphagia and inadequate sleep may be a reason for inc prevalence of obesity
- Stimulates wakefulness and appetite
- Inc metabolism.
- Nb narcolepsy deficiency of orexin. Link between wakefulness and food searching.
- Less sleep when on caloric restriction

Summary of events in arcuate nucleus.

Activation of NPY leads to inhibition of melanocortins



Obesity

Causes

- Psychogenic - habituation, depression
- Hypothalmic damage/dysfunction - almost never seen
- Genetic factors - animal studies, twin studies
- Childhood overnutrition - adipose cell number ↑

Effects

- Hyperinsulinaemia
- Insulin resistance
- Hypercortisolaemia
- Hypertension
- Thrombosis

Inanition (opp.of obesity)

Some causes (developed world)	Effects
anorexia nervosa	osteoporosis, bradycardia, hypotension, arrhythmias, amenorrhea, anaemia, leukopenia
(CNS lesions of hypothalamus)	