

## Brain mechanisms: Evidence

- Hunger and satiety signals arise from periphery and reach the brain.
- Eating and drinking are evolutionarily ancient (brain stem)
- Control mechanisms do not require the cortex. Decerebrated animals
  - Cannot seek food
  - Can eat, can respond to hunger and thirst
  - Can differentiate different kinds of food
  - Can vomit/reject bad food: area postrema is intact

## Hypothalamus

- Lateral hypothalamus
  - Control hunger
  - Lesion > decrease eating/drinking and body weight
  - Stimulation > increase eating/drinking
  - Block glutamate transmission > decrease food intake
  - LH needs inputs > Hunger and food intake are active processes
- 2 types of neurons producing
  - melanin concentrating hormone (MCH)
  - Orexin (hypocretin)
- Food deprivation increases MCH. Satiety decreases MCH
- 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
- NeuroPeptide Y (NPY)
  - NPY injections in hypothalamus: eating frenzies. Rats will tolerate pain in order to eat > NPY increases motivation to eat
  - NPY from Arcuate nucleus (in hypothalamus, near 3<sup>rd</sup> ventricle)
  - NPY secretion is triggered by brain stem nuclei and controlled by stomach secretions (Ghrelin)
  - Endocannabinoids act NPY. Marijuana used to increase appetite in chemotherapy patients

## Lateral hypothalamus/hunger summary

- Stomach (Ghrelin)/ brain stem (liver) > Arcuate (NPY) > lateral Hypothalamus > 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-4R receptor

- Satiety

- Leptin > NPY/ CART > MCH/Orexin

### Leptin

- Hereditary leptin deficiency (OB-like) in humans. Genetic deficit in the production of Leptin
- Leptin no longer used in weight loss diets: leptin resistance

### Ingestive disorders

- An increasing problem: obesity > Diabetes
- Type 1 diabetes: deficiency in insulin production (requires injections)
- Type 2 diabetes: deficiency in insulin receptors (treated with pills)

### Ingestive behaviors: obesity

- Average energy consumption
- 20% muscles, 20% brain, 60% heat and digestion
- 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 and above: Morbidly obese
- why people overweight?
- On average: 2,500 kCal in, but only 300 kCAL out
- Kind of foods eaten: high fat. High sugar. High calories
- Not enough activity (1/3 of what we should be doing)
- Overwriting of physiological signals for satiety: encourage 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 diet)
- Epidemiological studies (study of populations)

### § Pima Indians in the US vs Mexico

- High metabolic rates > increases availability of calories
- Spent if needed, stored if not

### Ingestive behaviors: obesity

- Mouse: obesity is due to leptin deficit
- Humans: no evidence for leptin production deficits but:

- Deficit in leptin transport through the BBB
- Deficit in sensitivity of leptin
- Treatments
- Exercise
- Wire in jaw (close the mouth) and liquid diet
- Gastroplasty: reshaping the stomach
- Intestinal bypass (directly to the large intestine)
- Gastric bypass. 35% success in long-term decrease in weight. Diminish secretion of Ghrelin
- Gastric bubble
- 5 HT promoters
- uncoupling protein (UCP). Convert nutrient to heat
- conclusions:
- eat slowly
- eat regularly
- exercise (not too much)
- don't eat at night

#### anorexia nervosa

- definition
- refusal to maintain weight over the lowest weight considered normal for age/height
- intense fear of gaining weight or becoming fat
- in women: three consecutive missed menstrual periods, without pregnancy
- 80% of cases are young women. 15% death rate
- can be due to too much exercise (too much exercise decrease hunger signals). Restricting food results in increase physical activity (weight loss)
- respond physiologically correctly to food > not a loss of interest in foods
- in normal > 6 months starvation has psychological consequences.

#### OCD?

- Genetic factors (evidenced by twin studies)
- Brain imbalance of NE, 5-HT AND NPY. No effective drug treatment

Treatment: psychotherapy