Appetite Regulation: Central Mechanisms

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What do we know?

- Body weight is biologically regulated
- Meal-to-meal and day-to-day energy regulation is primarily governed by gut hormones
- Week-to-week energy regulation is primarily governed by leptin which is produced in adipocytes
- Weight loss is associated with metabolic regulation in gut hormones and leptin that are intended to drive energy stores back to initial replete levels
Learning Objectives

• Describe the mechanisms of body weight control and appetite regulation

• Discuss the functions of
  • Satiation signals (gut hormones)
  • Adiposity signals (leptin)
  • Central regulation
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Model summarizing appetite control
Hypothalamic Regulation of Energy Balance (yin-yang system)
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Neuron Populations in the ARC

(Yin-Yang)

Two neuron populations with opposing effects on food intake in the hypothalamic arcuate nucleus (ARC):

- **Stimulate food intake**
  - NPY (neuropeptide Y)
  - AgRP (agouti-related peptide)

- **Suppress food intake**
  - POMC (proopiomelanocortin)
  - CART (cocaine- and amphetamine-regulated transcript)
The Importance of the Hypothalamus in Appetite Regulation

- Injury or lesions in the hypothalamus may result in a pattern of weight gain that is characterized as abrupt in onset and rapidly accelerating = hypothalamic obesity (HO)

- Causes include
  - Craniopharyngioma
  - Head trauma
  - Sarcoidosis
  - Aneurysm
  -- Meningioma
  -- Metastasis
  -- Surgery
  -- Radiation
A Case of Hypothalamic Obesity (HO)

Patient was asked to plot her weight over time

Your Weight Gain

- Cranectomy
- GH replacement started
- Starting steroids
- Now

Weight

Time
Hypothalamic Appetite Regulation

Farooqi S. Cell Metab 2006;4:260-262
Hypothalamic Appetite Regulation

6% of children with severe obesity had a mutation in the MC4 receptor.

3% of subjects with severe early onset obesity had a LEPR mutation.

Farooqi S. Cell Metab 2006;4:260-262
Hypothalamic Response to High Fat Diet; Inflammation may reduce responsiveness to normal neuropeptide signaling
Model summarizing appetite control
Reward or Hedonic Signaling
Activation of Regional Brain areas by Visual Images of Foods

Appetite regulation and energy balance is governed by a ‘yin-yang’ system of neuropeptides

POMC/CART are anorexigenic while NPY/AgRP are orexigenic

Orexigenic pathways predominate: “the gas peddle is always on”

Gut peptides and leptin mediate the relative release of the primary neuropeptides, thus maintaining energy balance and homeostasis

The hedonic reward pathway is responsible for food seeking behavior which often ‘overrides’ the homeostatic pathway (Thanksgiving!)
Summary of Key Learning Points of the Appetite Regulation Modules

• Appetite is biologically regulated by an intricate integration of gut hormone and leptin signaling, that act on neuropeptides within the brain
• Two regulatory systems, the homeostatic and hedonic pathways, influence our eating behavior
• That pathways also help to defend our body weight when patients try to lose weight