

Homeostasis: Active Regulation of Internal States

Chapter 13

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Internal States

Over the course of evolution numerous factors have contributed to maintaining an optimal internal state in the context of ever changing external factors.

Internal State	
Food energy	Fat Storage
Temperature	Nutrients
Fluid Balance	Hormones

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Modern World

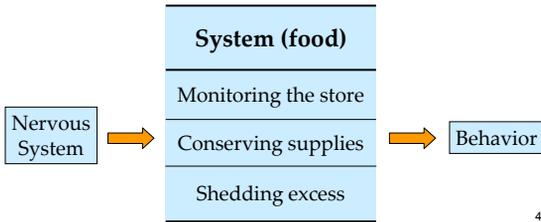
Optimal maintenance of internal states in modern times have been jeopardized.

Fat Regulation (obesity)	
Diabetes	Back problems
Heart Disease	Hormonal problems
Stroke	

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Redundancy

The homeostatic mechanisms are build around redundant systems. So if one fails the other can take over.

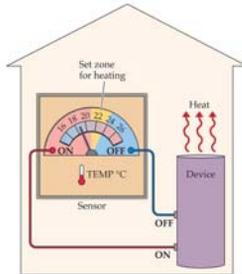


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Negative Feedback

Homeostatic systems are maintained by negative feedback system.

1. Set Point (set range)
2. Sensing device
3. Regulatory device



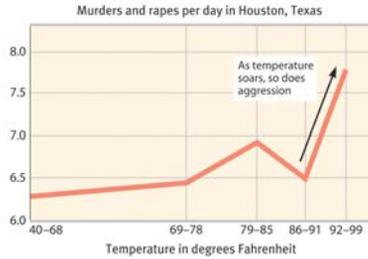
Temperature Regulation

All body chemical reactions are temperature dependant. Too low temperatures and these chemical processes slow down or even stop.
And higher temperatures mean protein molecules enmesh and don't function properly.

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Environmental Temperature

Environmental temperature can lead to aggressive acts. Murders and rapes increased with temperature in Houston.



Acquisition of Heat

Animals use different methods to regulate body heat. Some regulate it largely from inside and some maneuver themselves to find environments' that are either higher or lower in temperature.

Endotherm	Warm-blooded
Ectotherm	Cold-blooded

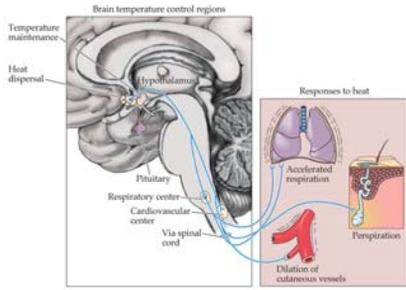
Evolution of Endothermy

Endothermy is a costly process. Why did evolution favor such a process?

1. More freedom and independence in locomotion.
2. Greater capacity of oxygen consumption and thus prolonged aerobic activity.

Metabolism

Breaking down of food leads to release of heat energy.



Heat Production

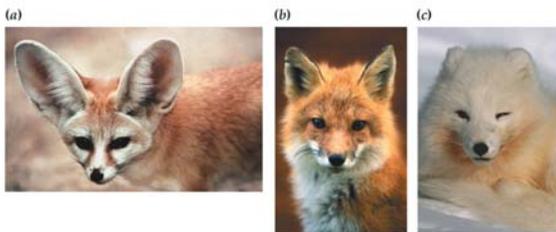
Release of heat per surface area.

TABLE 13.1 Body Size and Heat Production of Some Birds and Mammals

Species	Body weight (kg)	Body surface (m ²)	Surface-to-weight ratio (m ² /kg)	Energy output per day		
				Total (kcal)	Per unit of body weight (kcal/kg)	Per unit of body surface (kcal/m ²)
Canary	0.016	0.006	0.375	5	310	760
Rat	0.2	0.03	0.15	25	130	830
Pigeon	0.3	0.04	0.13	30	100	670
Cat	3.0	0.2	0.07	150	50	750
Human	60	1.7	0.03	1500	25	850
Elephant	3600	24	0.007	47000	13	2000

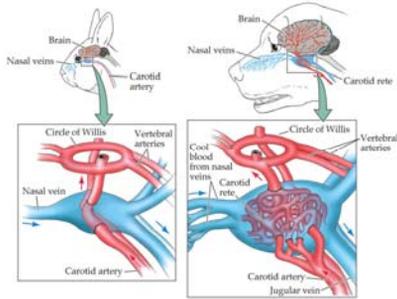
Insulation

Evolutionary ways of regulating heat.



Carotid Rete

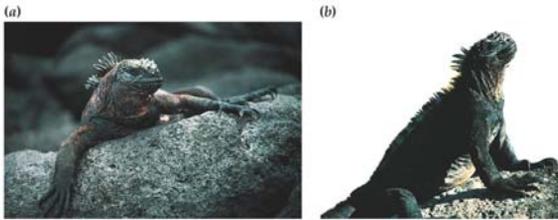
Specialized ways of regulating temperature



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Ectotherms

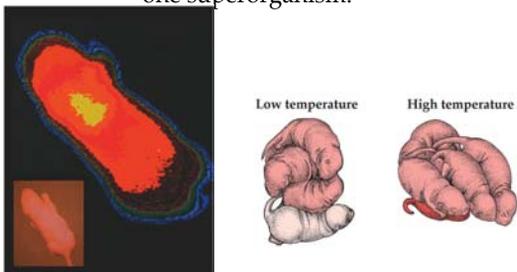
Harnessing the heat from the sun.



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Superorganism

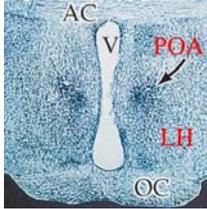
Heat regulation in multiple animals working as one superorganism.



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Hypothalamus

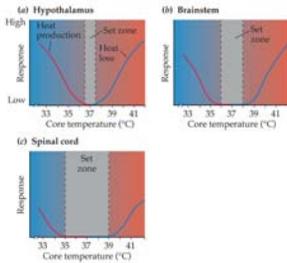
Preoptic area (POA) in the hypothalamus regulates conscious control of heat regulation and lateral hypothalamus (LH) autonomic responses.



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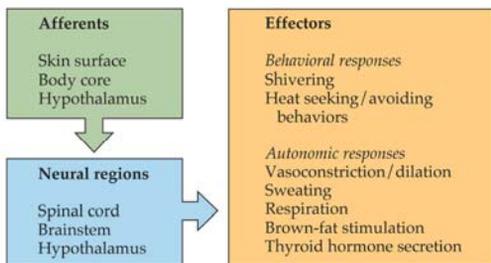
Hypothalamus

Multiple regions in the nervous system maintain different set zones to regulate temperature.



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Afferents to Effectors



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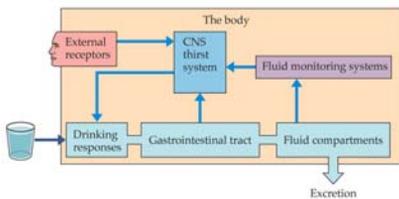
Fluid Regulation

1. Cells in the sea are surrounded with homogeneous concentration of salt, so salt inside the cells is easy to maintain.
2. Multicellular organisms came out of the sea so they had to maintain salt balance by avoiding dehydration thus developed watertight membranous seals.
3. Salt water in these cells is similar to sea water.

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Fluid Regulation

4. Watertight seals are difficult to make and water and salt is used by the body. Water and salt are lost and are replenished, so there has to be a monitoring device.



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Daily Water Balance

TABLE 13.2 Average Daily Water Balance

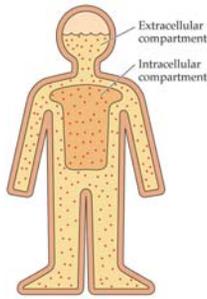
Source	Quantity (liters)
Approximate intake	
Fluid water	1.2
Water content of food	1.0
Water from oxidation of food	0.3
Total	2.5
Approximate output	
Urine	1.4
Evaporative loss	0.9
Feces	0.2
Total	2.5

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Two Compartments

The body contains two kinds of compartments

1. Intracellular
2. Extracellular

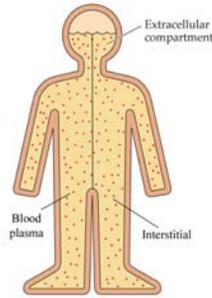


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Extracellular Compartment

The extracellular compartment is subdivided into two compartments

1. Interstitial
2. Blood plasma



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Kinds of Thirst

There are two kinds of fluid deficits in the body. One leads to reduction in extracellular compartment called **hypovolemic** thirst and the other in intracellular compartment called the **osmotic** thirst.

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Hypovolemic Thirst

1. Hypovolemic thirst can result from blood loss, vomiting and diarrhea.
2. Which result in extracellular fluid loss.
3. Blood pressure drops and baroreceptors in arteries send signals to the brain to constrict arteries.
4. Vasopressin is released and kidneys are instructed to reduce flow of water to bladder.

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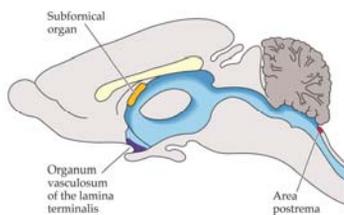
Hypovolemic Thirst

5. Also adrenal glands secrete steroid hormone aldosterone, that conserves sodium in kidneys.
6. Kidneys release renin which results in Angiotensin II that lead to water conservation.

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Circumventricular Organ

Angiotensin II through blood flow reaches subfornical organ and OVLT and initiates drinking and reduction in water release.

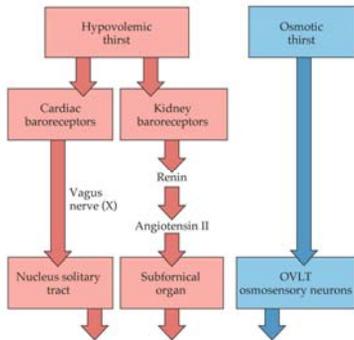


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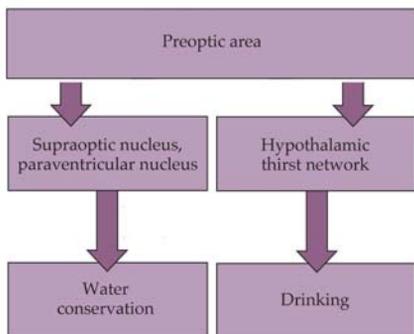
Osmotic Thirst

1. Common way to trigger thirst is through respiration, perspiration, and urination.
2. This results in reduction in solute (salt) from extracellular compartment.
3. Water from cells (intracellular compartment) is pulled out. Cells can get damaged.
4. Hypothalamus may contain osmoreceptors that monitor higher salt concentration and cause drinking behavior.

Summary



Summary



Food Regulation

1. Food is a source of energy and nutrients that build and maintain our bodies.
2. Hunger is a compelling motive and flavors are powerful reinforcements.
3. Of the 20 amino acids 9 need to be acquired from dietary sources.

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Energy

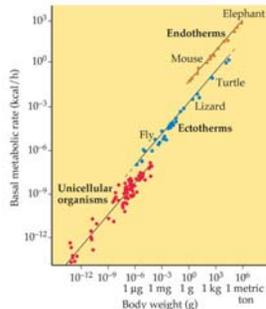
1. All the energy used to move, think, breathe and maintain body temperature is gotten from food. We “burn” food similarly as we burn fuel in a car.
2. Some energy in food cannot be converted into metabolic form. Seventy-five percent of energy is used in three functions:
 1. New food digestion
 2. Basal metabolism
 3. Active behavior

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Basal Metabolism

The expenditure of energy for active behavioral processes show elasticity. Basal metabolism follows the following equation:

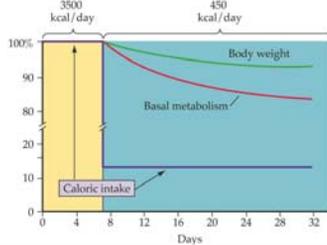
$$\text{Kcal/day} = 70 \times \text{weight}^{0.75}$$



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Basal Metabolism

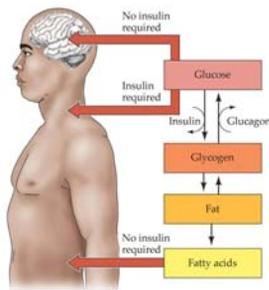
Even though energy expenditure will change basal metabolism (15%) and body weight (6%) but these changes are meager.



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Carbohydrates and Energy

Large carbohydrates molecules are broken down into small carbohydrates including sugars. Most important sugar is **glucose**, used by the brain. Other body cells use glucose and **ketones**. Energy is stored in the liver as **glycogen** with insulin and turned into energy by **glucagon**. Long-term fat store is **adipose tissue**.



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Insulin and Energy Use

Insulin converts glucose into glycogen, and enables the body to use glucose. Food is broken down and glucose is released into the bloodstream. Insulin is released to use glucose.

1. **Cephalic Phase:** Stimuli from food evoke a conditioned release of insulin in anticipation of glucose.
2. **Digestive Phase:** Food entering the stomach and intestines releases gut hormone which stimulates insulin.
3. **Absorptive Phase:** Glucoreceptors detect circulating glucose and signal pancreas to release insulin.

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Insulin and Glucose

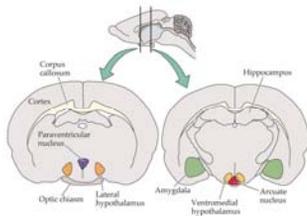
Insulin and glucose are not the only signals to hunger or satiety.

1. Inject large amounts of insulin in animals and they still eat.
2. Untreated diabetic rats eat large amounts of food (glucose) but ate normally if given high-fat diets.

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Hypothalamus

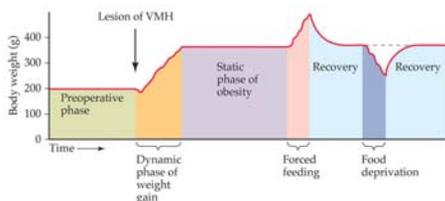
Old model of hunger and satiety is based on two centers of hypothalamus, viz., lateral hypothalamus (LH, hunger) and ventromedial hypothalamus (VMH, satiety).



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VMH

Ventromedial hypothalamic destruction led to obesity (*hyperphagia*) in rats. However, the obesity was of two types dynamic and static. Weight increased first and then stabilized. So some other center was regulating satiety signals.



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LH

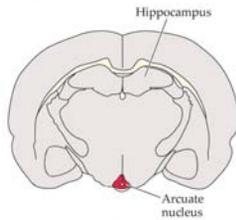
Lateral hypothalamic destruction led to *aphagia*, refusal to eat, in rats. But LH destruction also led to *adipsia*, refusal to drink. However, if kept alive through a feeding tube rats recovered their body weight suggesting other centers in the brain may regulate hunger.

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Arcuate Nucleus

More recent research has suggested that arcuate center in the hypothalamus by interacting with different hormones:

1. Insulin
2. Leptin
3. Ghrelin
4. Peptide YY₃₋₃₆



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Leptin

Fat cells produce leptin (Greek leptos: thin) that enter the blood stream to affect hypothalamus, choroid plexus and other cortical regions that monitor energy reserves in the form of fat.



Zucker rats with ob/ob genes

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Ghrelin

Ghrelin is a potent appetite stimulant, its levels rise during fasting and drop right after a meal.

Introduction of ghrelin in humans and rats increases eating behavior.

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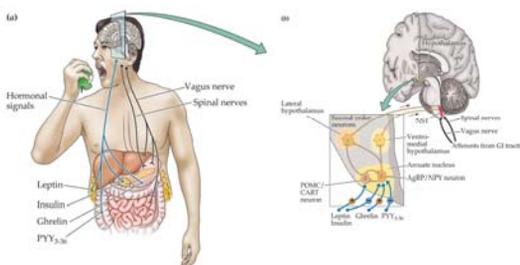
Peptide YY₃₋₃₆

PYY₃₋₃₆ is a potent appetite-suppressant stimulus to the hypothalamus. Secreted by cells in the small and large intestines curbs appetite.

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Summary

How different hormones affect hunger and satiety.



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Obesity

Obesity a growing problem worldwide is difficult to treat. About 65% of people in the US are over weight and about 31% obese (Flegal, et al., 2002). Strategies to curb obesity include:

1. Appetite control
2. Increased metabolism
3. Inhibition of fat tissue
4. Reduced absorption
5. Reduced reward

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Appetite Control

A lot of effort has been directed toward controlling appetite by drugs that affect hypothalamus system, with little improvement in the condition for obese individuals.

1. Leptin appears to effect cannabinoid levels in the hypothalamus increasing appetite. If cannabinoid receptors can be blocked hunger could be suppressed.
2. Melanocortin receptor (MC4R) may be an important receptor in regulating hunger. Fenfluramine affects melnocortin pathway.

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Appetite Control

3. PYY₃₋₃₆ may be another hormone that is low in obese patients. Supplementary PPY₃₋₃₆ may reduce calorie intake in patients by one-third.

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Increased Metabolism

An alternative approach to treating obesity involves treatments that cause the body's metabolic rate to increase.

Thyroxine has been used to increase metabolism with undesirable consequences (heart rate increase). Special compounds are now being developed to affect thyroid hormones receptors (TRb) and not (TRa).

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Fat Tissue

Fat tissue requires new blood vessels. When these blood vessels are blocked (angiogenesis inhibitors) fat tissue does not develop.

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Reduced Absorption

Orlistat interferes with absorption of fat. The drug has modest effects and cause intestinal discomfort.

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Reduced Reward

Drugs that affect brain's reward circuitry reducing the rewarding properties of food may prove beneficial to weight loss.

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Eating Disorders

1. **Anorexia Nervosa:** Anorexia (no appetite) nervosa (NS related) is a eating disorder where the individual perceives herself to be overweight, when in fact she is not. A fatal disorder leads the individual to eat less and less.
2. **Bulimia Nervosa:** Bulimia (great hunger) another fatal disease involves individuals to gorge themselves with "junk food" and relieve themselves later on with vomiting or laxatives.

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