WEIGHT CONTROL AND OBESITY

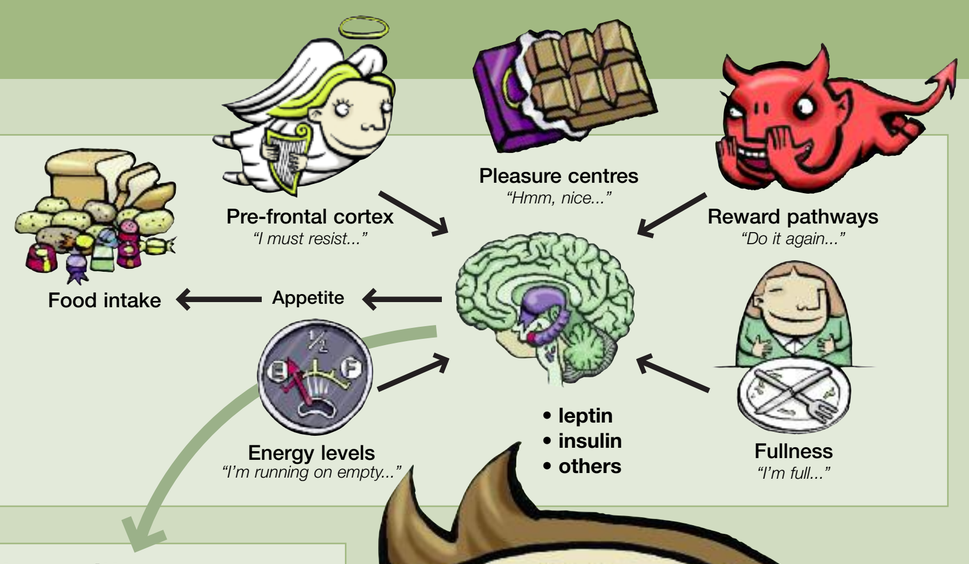
The food we eat supplies us with energy; we use energy through metabolic activity and exercise. Any excess energy is stored. As a population our energy intake is going up and our energy use is going down. The result? An alarming increase in the numbers of people overweight or obese. We now know that the hypothalamus is the key weight control centre in the brain. But appetite is sensitive to many factors. How do we know when we have eaten enough? What effect does our family environment have? How are lifestyle changes affecting energy use? What if we run low on energy? And how are we affected by media representations?

In the brain...

The **hypothalamus** (red area) integrates signals from the body and from other parts of the brain. **Leptin** provides information about the body's energy stores. **Pleasure centres** relay messages that certain food is enjoyable; **reward pathways** encourage us to repeat actions that have been good for us in the past.

Messages from the pre-frontal cortex, the 'thinking' part of the brain, carry our conscious desires (e.g. to resist temptation). The end result is our '**appetite**' – our drive to eat.

How this all happens is not clear. Various **neurotransmitters** are known to be important, either increasing or reducing hunger.



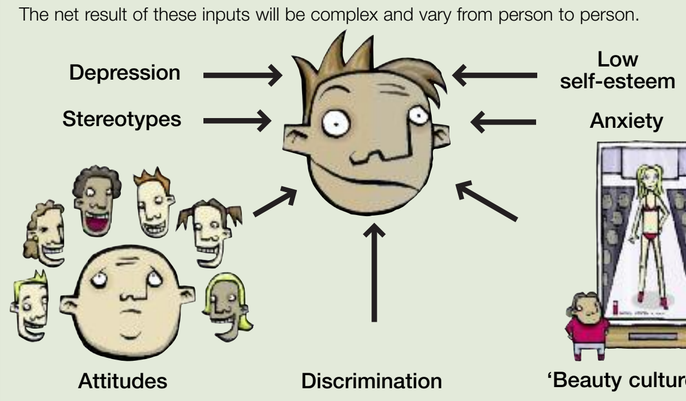
Psychological factors...

Food intake is responsive to our mental state as well as our physiological needs. Depression or low self-esteem may lead to 'comfort eating'.

Strong social pressures exist. We are constantly being told that 'beauty = slimness', while seductive diets promise perfect figures.

Overweight people suffer from discrimination, ranging from bullying and name calling to worse job prospects.

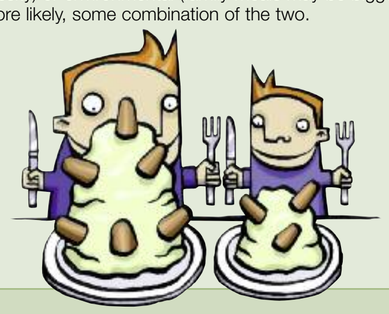
The net result of these inputs will be complex and vary from person to person.



Developmental factors...

If we are very small when born (e.g. because our mother's nutrition was poor), it seems that our **hormone systems** develop such that we are more likely to become obese when we are older.

Family environment has a big influence. Children growing up with obese parents are much more likely to become obese. This could be a genetic effect (sharing genes predisposing to obesity) or environmental (family meals may be bigger) or, more likely, some combination of the two.



Neurotransmitters...

Eat more...
NPY
AGRP
Orexin
Cannabinoids

Drug
Sibutramine
Rimonabant

Eat less...
Serotonin
Norepinephrine
αMSH
Others

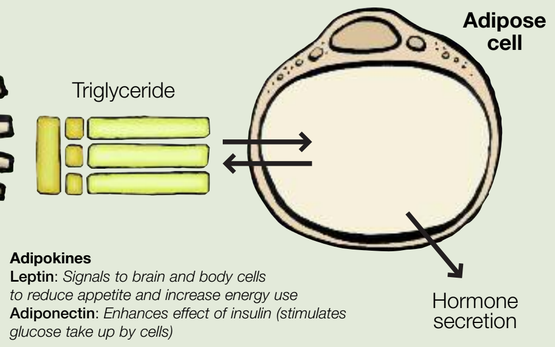
Some neurotransmitters are involved in increasing appetite, others in reducing it. Some are the targets for drugs (see above); others are affected by genetic variation (e.g. a gene called MC4R affects αMSH).

In adipose tissue...

Adipose (fat) cells are bags of fat molecules waiting to be mobilised and burned.

Adipose tissue also releases hormones (**adipokines**), which affect how the body uses energy and act on the brain to alter appetite.

The role of adipokines is not well understood. Large deposits of adipose tissue, though, seem to disrupt their normal function.



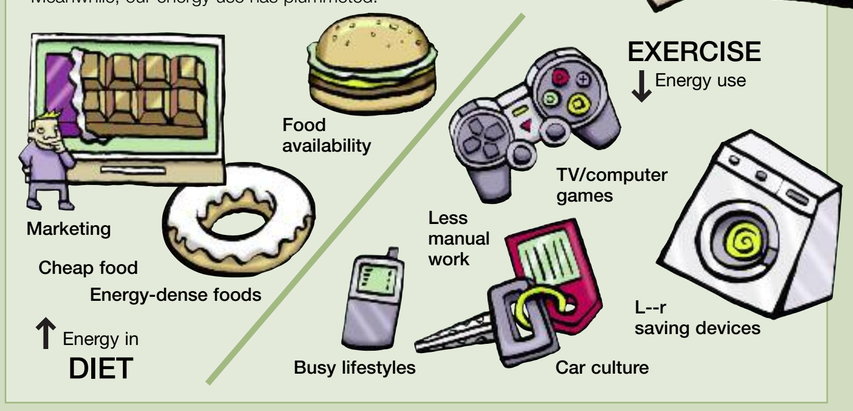
Adipokines
Leptin: *Signals to brain and body cells to reduce appetite and increase energy use*
Adiponectin: *Enhances effect of insulin (stimulates glucose take up by cells)*

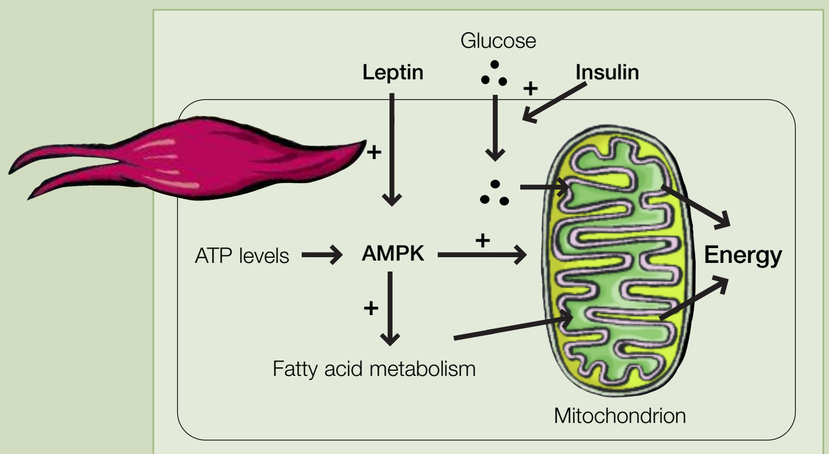
Inflammatory mediators: *Promote inflammatory state*

Social factors...

Modern life has a strong influence on food intake and energy use. Energy-dense food is all around us and fiercely marketed.

Meanwhile, our energy use has plummeted.





In muscle cells...

Energy levels must be controlled within each individual cell and in the body as a whole.

A key sensor is a molecule known as **AMPK**, which monitors levels of the cell's 'energy currency', ATP. If a cell is running short of energy, AMPK prompts mitochondria to make more ATP.

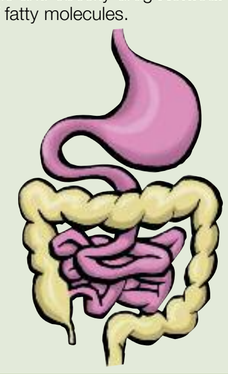
This system is sensitive to the needs of the body. AMPK responds to leptin, which drives up cellular metabolism, using up more energy.

Many genetic influences affect these complex cellular systems. Some mutations make cells less responsive to leptin; others alter fatty acid metabolism in the cell. Some factors alter AMPK action.

In the digestive system...

The stomach and digestive system sense when food has been eaten, relaying messages to the brain – via stretch receptors and nerve impulses and through a complex network of hormonal signals. These, for example, create the sensation of feeling 'full'.

The anti-obesity drug **Xenical** works on the gut, inhibiting the uptake of fatty molecules.

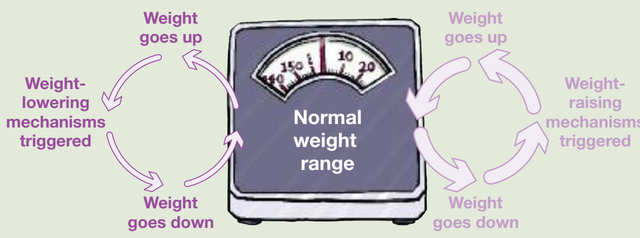


HORMONES

↓ Hunger	↑ Hunger
Cholecystokinin	Ghrelin
PYY3-36	Others
Others	

NERVOUS SYSTEM

Vagus nerve
(controls movement of food through the digestive system)



Weight control comprises a set of checks and balances, a homeostatic mechanism designed to keep our weight within certain limits. In the last 20–30 years in Western society, these biological mechanisms have come into conflict with an environment where food is plentiful and energy use has plummeted.

Dieting to lose weight can be successful, but is difficult. The most effective methods involve realistic goals, a balanced, calorie-controlled diet, an exercise programme, and support from a medical professional.

Like other homeostatic systems, weight control is largely subconscious. We can consciously control weight to some extent, but it is also subject to powerful biological forces.

It is possible to interfere with any part of the weight-control system – pharmaceutical approaches alter metabolism; political changes alter the environment we live in. But no part exists in isolation. Obesity is a complex issue, only partly understood.

Glossary

Adipokines: Hormones produced by adipose tissue. Have a variety of effects on the body's use of energy and storage. New ones are still being discovered.

AMPK: AMP-activated protein kinase. Intracellular enzyme, important in controlling cell's energy use. Key link between body's overall energy status and activity within the cell.

Homeostasis: The balanced state of the living body (including temperature, chemistry, blood pressure, sleep and wakefulness etc.), despite variations in the environment.

Hypothalamus: Small area at the base of the brain responsible for many aspects of homeostasis. Integrates body and brain signals to control eating behaviour.

Insulin: Hormone produced by the pancreas that regulates blood sugar levels and sugar uptake by cells.

Leptin: Hormone produced by adipose tissue that regulates appetite. Has complex effects on body cells and the brain.

MC4R: Melanocortin 4 receptor: Protein found on neurons in the hypothalamus. Activation of MC4R leads to a drop in appetite. Mutations in MC4R account for some cases of severe obesity.

Neurotransmitters: Chemicals that transmit nerve signals across synapses.

Rimonabant: A drug in development that suppresses hunger and the urge to smoke.

Sibutramine: Obesity drug that acts in the brain to regulate appetite.

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