Detailed Study Notes: Episode 458

How Foods Impact Satiety, Hunger & Appetite

Table of Contents

Introduction to this Episode

Given the negative consequences of consistent overconsumption of food (leading to a caloric surplus), having a dietary intake that is of appropriate calorie intake is an important aspect of long-term health. Therefore, thinking about which foods and diets can help promote appropriate satiety to keep calorie intake in check is a key focus for many researchers and practitioners.

There is a complex system of human appetite control. This appetite system influences food consumption and associated motivational drives such as hunger, as well as interacting with and being influenced by energy expenditure. Satiety is an important psycho-biological process involved in the expression of human appetite, inhibiting hunger and intake following food or beverage consumption.

In this episode, the Sigma team discusses the human appetite system, how different nutrients and foods impact satiety, and the implications of this research.

Connection to Previous Episodes

This episode touches on ideas raised in several previous episodes:

1. This episode mentioned work on the appetite system from the University of Leeds, done by Dr. Mark Hopkins and colleagues. Dr. Hopkins was on the podcast in episode 299 to discuss the interaction between energy intake and expenditure, including how physical activity impacts appetite and calorie intake.
2. The regulation of energy intake was discussed in episode 391, in which Alan and Danny looked at the primary models of body mass regulation.
3. In episode 429, Drs. Kevin Hall and Stephan Guyenet discussed two proposed models of obesity pathogenesis: the Carbohydrate-Insulin Model and the Energy Balance Model. In that episode, the central role of the brain in controlling intake was discussed, as well as the impact of food reward and palatability on food intake.

What are Appetite, Satiety & Satiation?

As summarized in a 2019 paper by Nuno Casanova and colleagues (the group at Leeds, including John Blundell & Mark Hopkins) :

> *"The **human appetite system** comprises a set of processes that influence energy intake (EI) i.e. food consumption and associated motivational drives such as hunger. This system interacts with and is influenced by energy expenditure (EE). Consequently, human appetite is best considered within an energy balance framework.*
>
> ***The essence of human appetite is that it links the internal (physiological) and the external (social, cultural, physical and psychological) environments.** Therefore, this interplay means that human appetite is an interactive biopsychological phenomenon."*

The inhibitory control of appetite is thought to be achieved via an array of adipose and gastrointestinal derived peptides that modulate hunger and satiety on a meal-to-meal (episodic) and day-to-day (tonic) basis.

Some key points from the Casanova *et al*., 2019 paper

1. Adipose tissue and gastrointestinal peptides modulate hunger and satiety.
2. Appetite does not appear to be under tight homeostatic control.
3. Energy deficit and weight loss may alter the strength of homeostatic feedback.

"Satiation and satiety are part of the body's appetite control system and are involved in limiting energy intake. **Satiation** is the process that causes one to stop eating; **satiety** is the feeling of fullness that persists after eating, suppressing further consumption, and both are important in determining total energy intake." - Benelam, 2009

Satiety is an important psycho-biological process involved in the expression of human appetite, inhibiting hunger and intake following food or beverage consumption. (Tremblay & Bellisle, 2015)

Satiation relates to the feelings of fullness that contribute to the decision to stop eating.

There can then be sub-types of satiety. For example:

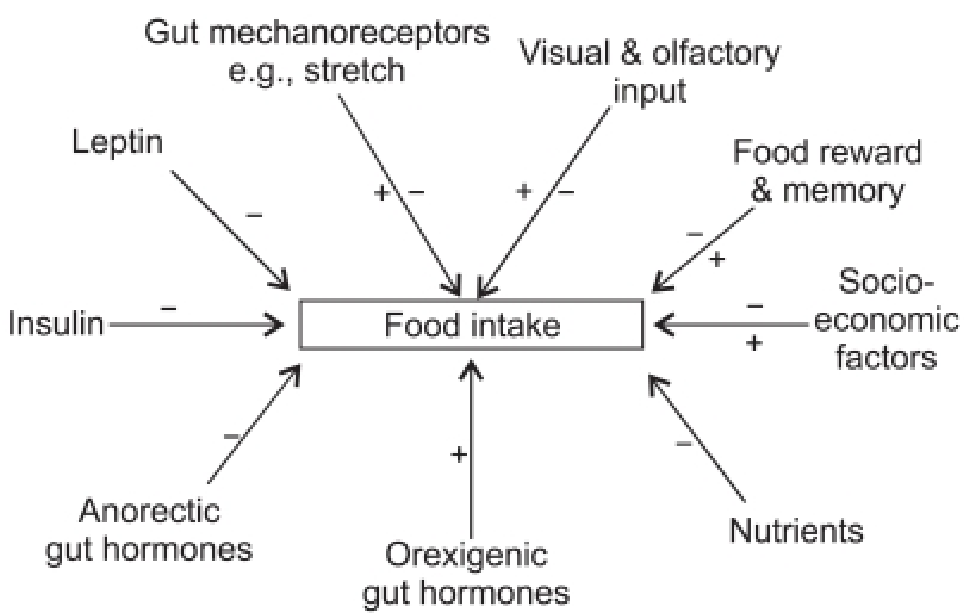
- Sensory-specific satiety – which is linked to eating specific foods, or a reduced satisfaction by continuously consuming a certain type of food, which is generally overcome when you are exposed to a new food or flavour.

- Early satiety – happens when you are unable to finish a meal or feel very full after small amounts of food. This is typically caused by an obstruction/blockage in the gut or in reflux disease.

Appetite Control

Fully understanding the regulation of energy balance is a complex challenge and has linked various research disciplines. e.g., endocrinology, gastroenterology, neurobiology.

The major determinants of appetite control:

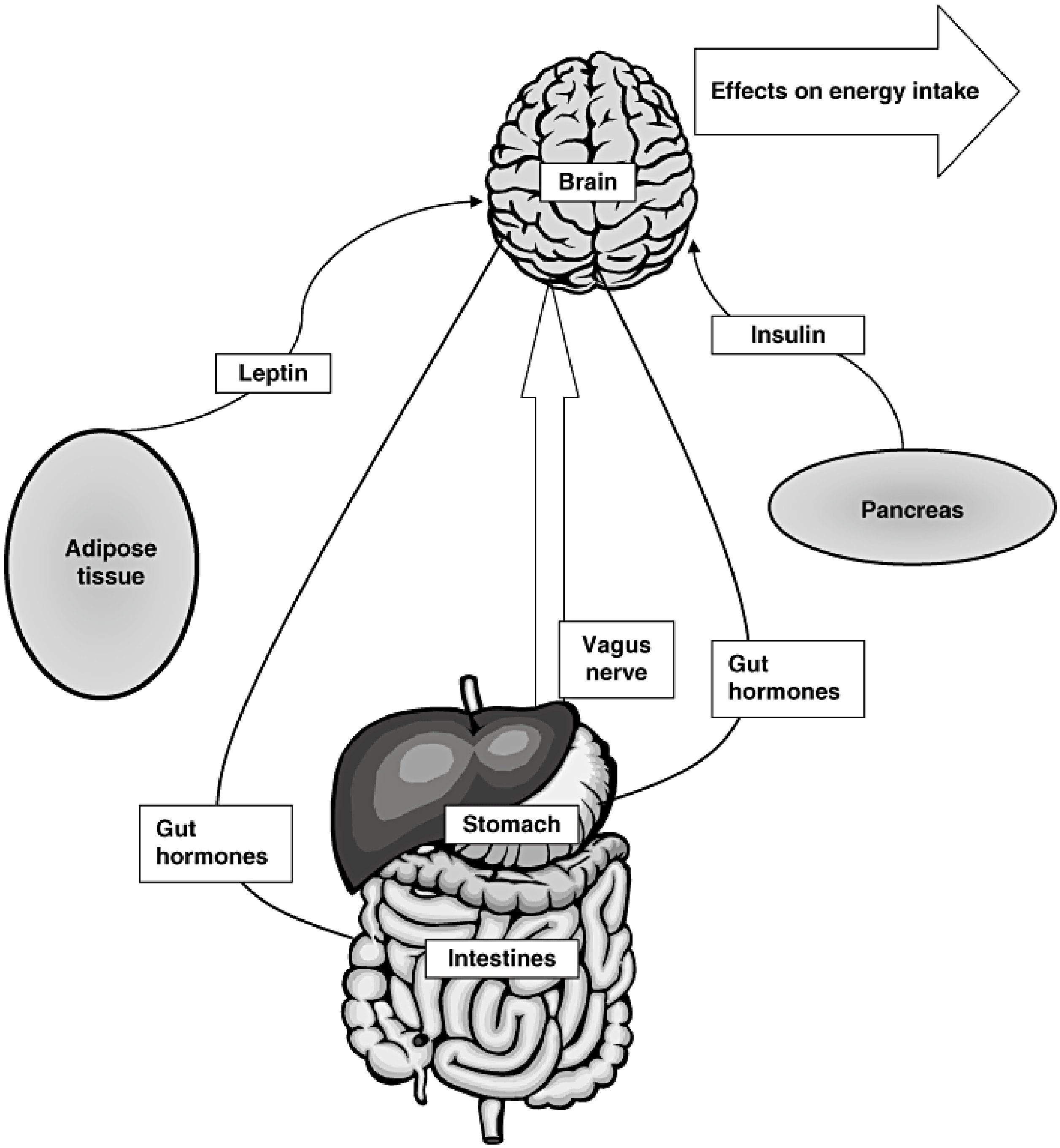


From: De Silva & Bloom, Gut Liver. 2012 Jan; 6(1): 10–20.

Role of the Brain

- The pathway begins in the hypothalamus, specifically in an area called the arcuate nucleus (or the ARC)
    - Note for later: Within the ARC, robust circadian rhythms in neuronal activity, clock gene/protein expression, and feeding-related neuropeptide expression has been demonstrated (Guilding et al., 2009)
- Neurotransmitters in key neurons of the hypothalamus regulate feeding behavior and body weight (Björn Meister, 2007)

- Two categories of neurons in the ARC that regulate appetite:
    1. orexigenic (stimulate feeding) neurons
    2. anorexigenic (inhibit feeding) neurons
        - E.g. pro-opiomelanocortin (POMC)



From: Benelam, 2009

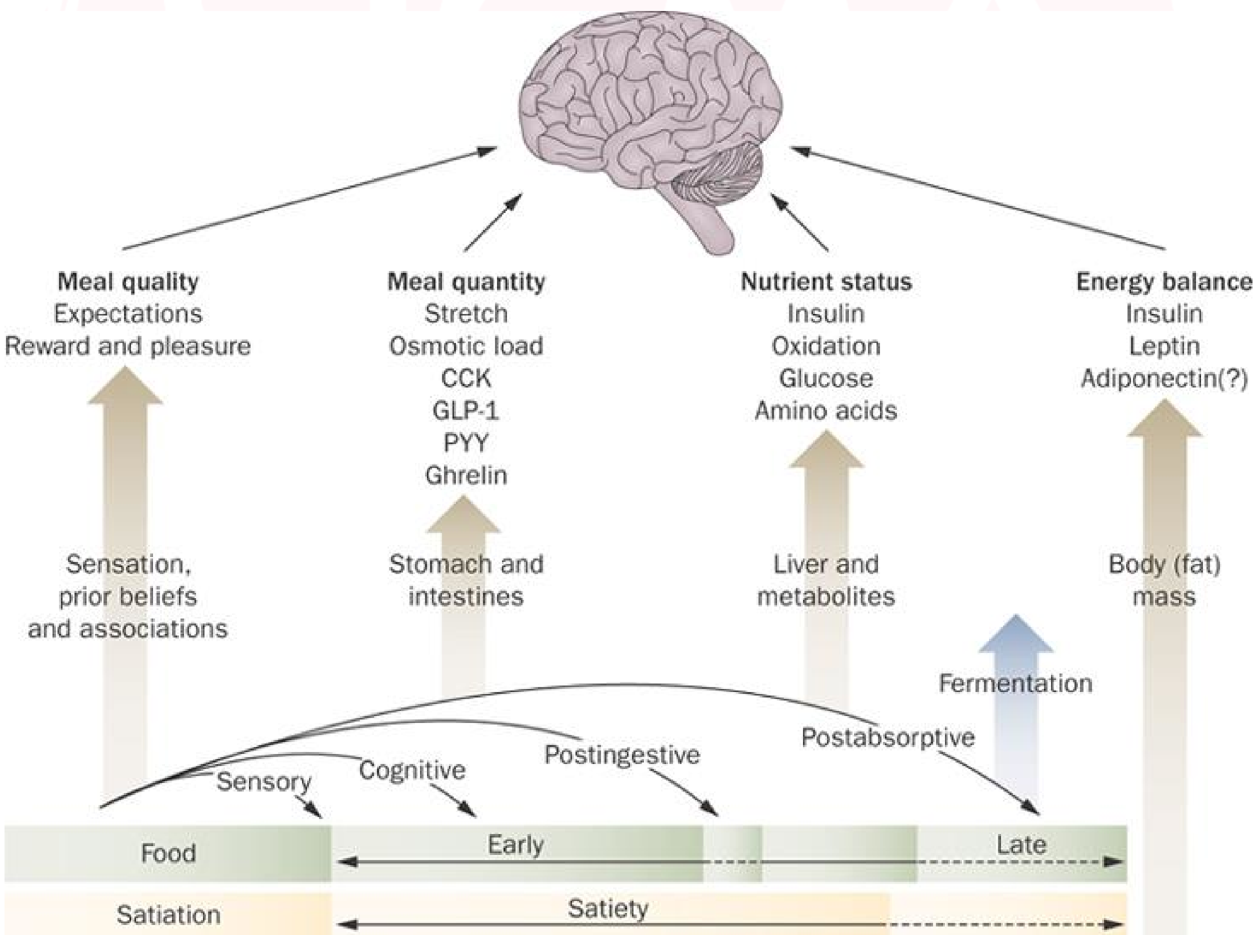
Role of Hormones

- **Leptin**
    - Produced in adipose tissue
    - Acts on receptors in the arcuate nucleus of the hypothalamus to promote satiety and induce thermogenesis
    - It is relative to the individual's amount of adipose tissue, and isn't really affected by how fatty a meal is
- **Cortisol**
    - Useful in response to acute stress
        1. E.g. Nudges our glucose stores to ensure the body has sufficient energy to respond to the stress
    - But… sustained stress leads to chronically elevated cortisol
        1. This suppresses leptin (or satiety response)
        2. Leads to an increased desire for foods dense in sugar and fat
- **CCK**
    - Satiety hormone 'cholecystokinin' (CCK)
    - Suppresses feeding
    - Its release is controlled by gut neurons and mucosa in the gut and microbiome
    - Stimulated by fatty acids, certain amino acids, and sugar
- **Peptide tyrosine-tyrosine (PYY)**
    - Produced in the L cells of the gut
    - After a meal, circulating levels endogenous PYY rise within 15 minutes, peak at about 90 minutes and remain elevated for up to 6 hours – Adrian et al., 1985
- **Glucagon-like peptide 1 (GLP-1)**
    - GLP-1 is released postprandially from gut L cells in proportion to the calories ingested
    - GLP-1 responds in 2 phases post meal:
        1. First peak occurs before nutrients/food reaches the distal gut
        2. It is believed the second peak is influenced by free fatty acids
    - The GLP-1 receptor is expressed in the pancreas, where GLP-1 functions as an incretin hormone
- **Ghrelin**
    - Produced in the GI tract
    - Commonly referred to as our hunger hormone
    - It increases hunger, decreases energy expenditure and stimulates cortisol release.

The Satiety Cascade

- Beyond just the metabolism of nutrients in the GI tract, various other aspects of food consumption impact appetite regulation.
  - Therefore, two foods of equal nutrient content can affect appetite differently.
- Over 25 years ago, Blundell et al. (1987) proposed a framework that describes the complex interaction between eating and appetite, called the **'satiety cascade'.**
- Updated revisions have been published since then, to take new findings into account.
  - E.g. Blundell, 2010
- The satiety cascade model predicts that:
  - Early pre-ingestive signals from cognitive and sensory processes are the main drivers of **satiation**.
  - Cognitive, sensory, post-ingestive, and post-absorptive signals are combined to determine the experience of **satiety**.

Satiety cascade from Blundell (image modified by Mela, 2006):



Taken from: Bilman et al., 2015

High and Low Satiety Phenotypes

- All foods induce satiety to a variable strength, but satiety responsiveness varies considerably from person to person.
- This led to the identification of high and low satiety phenotypes.
- These phenotypes show marked differences in major satiety markers following either a low-energy density or a high-energy density meal.
- The "low-satiety phenotype" is associated with greater eating disinhibition and reported self-control over food cravings (Dalton et al., 2015).
- For more on this, see: Cooling & Blundell (1998) - Are high-fat and low-fat consumers distinct phenotypes? Differences in the subjective and behavioural response to energy and nutrient challenges

Impact of Diet

There are several components of diet that may influence satiety. These include:

1. Impact of Macronutrients
    a. Protein
    b. Fibre
    c. Carbohydrates – CIM
    d. Fat
2. Impact of Foods
    a. The Satiety Index
    b. Energy Density
    c. UPFs
    d. Solid vs Liquid Meals
3. Impact of Timing
    a. Time of day/ circadian effects
    b. Meal frequency
    c. Food order in a meal

Protein

Protein has been the macronutrient of interest as research indicates that increasing the protein composition of the diet, without changing the net energy load, can lead to enhanced feelings of satiety.

- Early evidence summarised by Douglas Paddon-Jones et al. (2008)

Van der Klaauw trial: High Protein Intake on GLP1 and PYY Release

- Agatha van der Klaauw et al (2013) published in Obesity
- Demonstrated if the meal is rich in proteins, there is a higher increase in circulating levels of GLP-1 and PYY in normal-weight subjects than if the meal is rich in carbohydrates or fats.
- PYY levels were highest after a high-protein breakfast
    - At 4 hrs: PYY was highest after the high protein breakfast compared to high fat or carb meal.
- GLP-1 levels were elevated after a high protein meal.
- However, the investigators did not find any differences in hunger scores ($P = 0.777$) or fullness scores ($P = 0.888$) between the different macronutrient manipulations.

Dietary Fat

Dietary fat affects satiety by (Little et al. 2007):

- Slowing gastric emptying
- Stimulating the release of satiating gut hormones
- Suppressing the release of ghrelin

The induction of physiological satiety signals may depend on the consumption of fatty acids in the particular fat consumed. Two features of fatty acids are:

1. Chain length
2. Degree of saturation
    a. Short-term studies indicate that PUFA may exert a relatively stronger control over appetite than MUFA and SFA
        i. Clare Lawton et al, University of Leeds (2020)

Carbohydrate

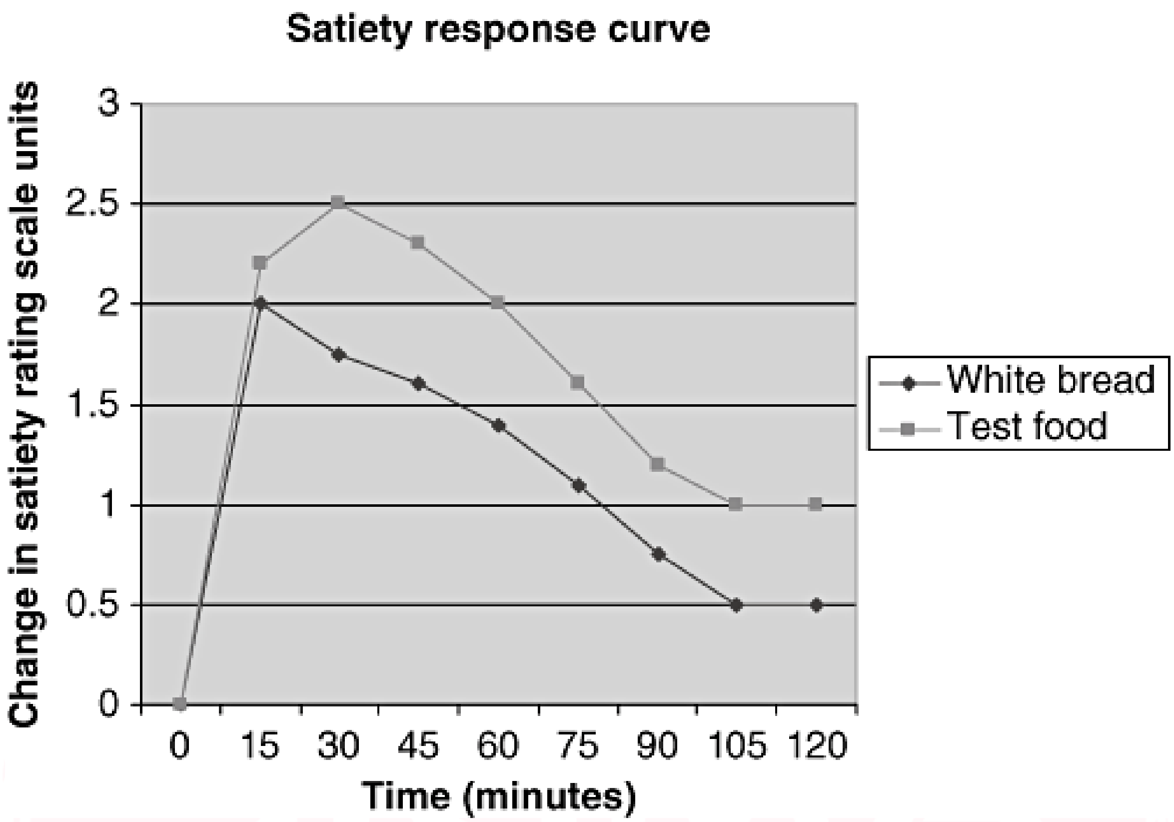
Current evidence suggests that, when other factors such as fibre content are controlled, GI does not have a significant effect on satiety (Benelam, 2009)

Some types of fibre can promote satiety, but this is highly dependent on the type of fibre.

- Viscous fibres, such as petin, or novel gelling fibres, usually alginates, appear to be the most satiating.

The Satiety Index

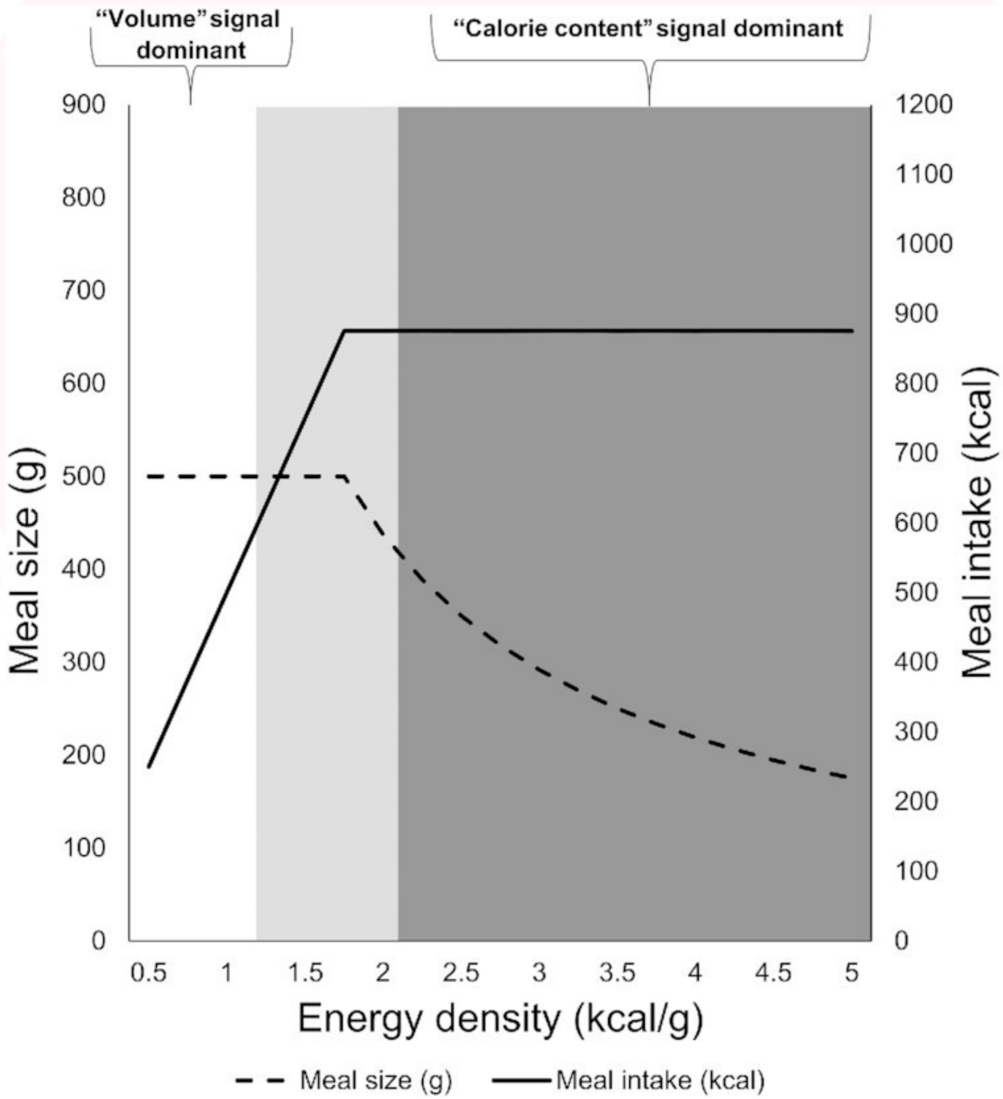
- Based on the work of Susanna Holt et al. (1995), published in the European Journal of Clinical Nutrition
    - A satiety index of 38 common foods with portions of comparative energy (240kcal).
- A list of foods that are given a number out of 100. White bread is the reference foods, ranked as "100".
- They obtained a satiety rating every 15 mins over a 2 hour period.
- A satiety index score was computed based on AUC for the satiety response curve for the test food by the mean satiety AUC for white bread *100.
    - So white bread had a satiety score of 100% and the test foods are expressed as a % of white bread
    - Example shown in the figure over the page
- Example of high satiety scores:
    - Boiled potatoes = 323
    - Ling fish = 225
    - Porridge/Oatmeal = 209
    - Oranges = 202
    - Apples = 197
- Example of low satiety scores:
    - Peanuts = 84
    - Mars candy bar = 70
    - Doughnuts = 68
    - Cake = 65
    - Croissant = 47
- Protein, fibre, and water contents of the test foods correlated positively with SI scores



From: [Benelam, 2009]

Energy Density

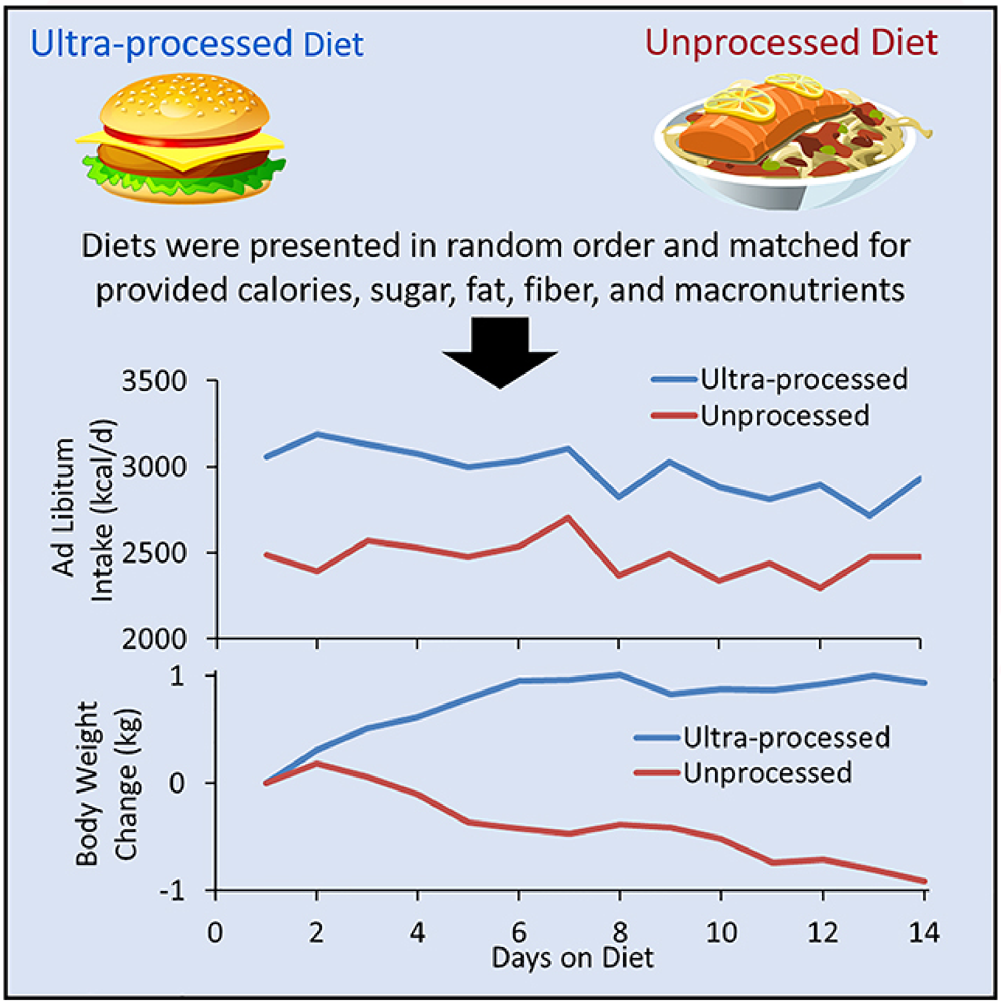
- There seems to be some sensitivity in humans to the energy content of foods, and thus impacting subsequent intake.
- Recent paper out of Bristol ([Flynn et al., 2022]())
    - Used data from NDNS and secondary analysis of Hall UPF trial - see section below
    - Suggested that: *"volume is the dominant signal with lower energy-dense foods and calorie content is the dominant signal with higher energy-dense foods"*
    - Using an 875 kcal meal as an example, the below figure shows how the energy density of a meal influences whether the dominant signal detected by the body is mainly due to the volume or the calorie content.



From: [Flynn et al., Am J Clin Nutr. 2022 Aug; 116(2): 581–588.]()

Ultra-processed Foods

- Hall et al. 2019 UPF RCT:
  - NIH Clinical Center and randomized to receive either ultra-processed or unprocessed diets for 2 weeks immediately followed by the alternate diet for 2 weeks.
  - Meals were designed to be matched for presented calories, energy density, macronutrients, sugar, sodium, and fiber.
  - Subjects were instructed to consume as much or as little as desired.
  - Energy intake was greater during the ultra-processed diet



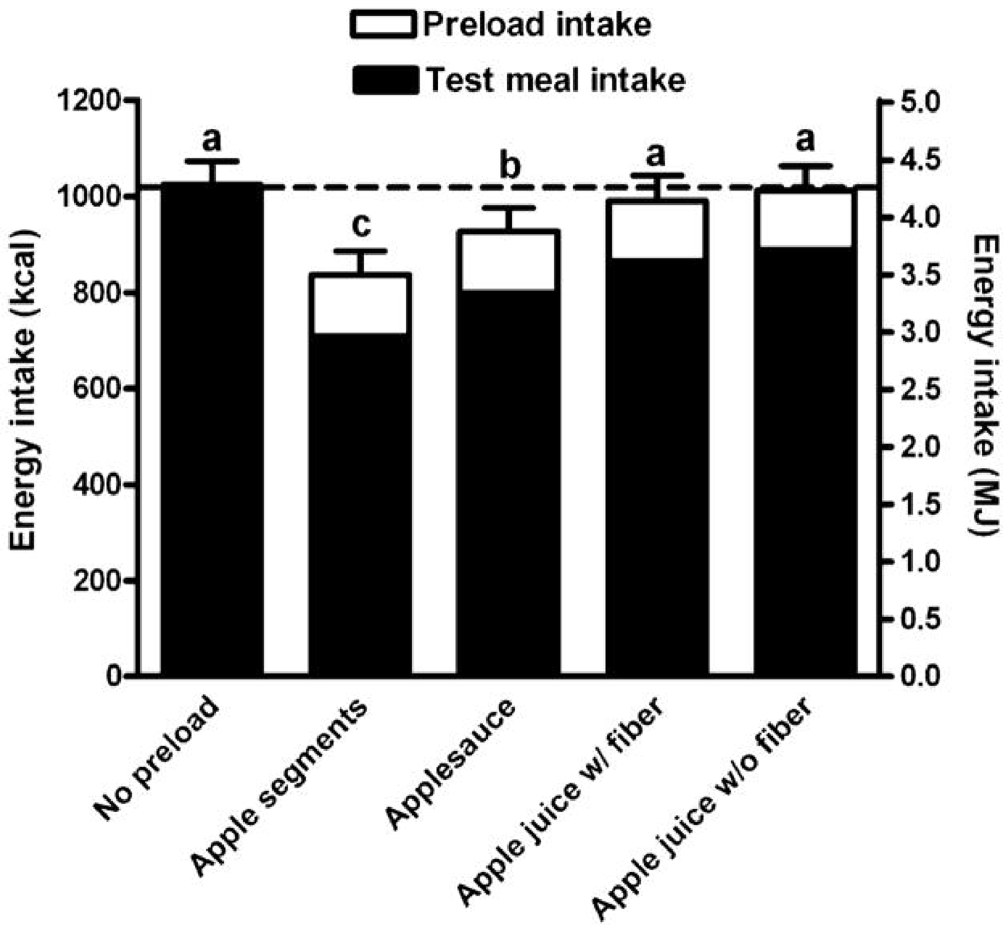
From: Hall et al., Cell Metab. 2019 Jul 2; 30(1): 67–77.e3.

However, it may be important not to see all UPFs in the same way

- e.g. Soy-based Meat and Dairy Alternatives likely not detrimental?

Solid vs Liquid Meals

- Food form can have an impact on satiety
- Sugar-sweetened beverages are easy to overconsume. One aspect of this may be that there is a lower satiety response than that seen with an equal amount of calorie and sugar from solid food
    - Pan & Hu (2011) review - Harvard - Effects of carbohydrates on satiety: differences between liquid and solid food
- Mattes & Campbell, 2009
    - Impact of apple in different forms
    - Compared the effects of 300-kcal loads of a:
        - Solid (apple)
        - Semisolid (apple sauce)
        - Beverage (apple juice)
    - The apple juice elicited the weakest appetitive response
    - The whole apple elicited the strongest appetitive response
    - Apple sauce impact was intermediate
- Barbara Rolls apple study (Flood-Obbagy & Rolls, 2009)
    - 5 weeks
    - Consumed preloads of apples in different forms prior to a meal:
        - Apple
        - Applesauce
        - Apple juice with added fiber
        - Apple juice without added fiber
    - Fullness ratings = apple > applesauce > both juices
    - Less calories consumed after eating whole apple (see figure over page)
    - Whole apple increased satiety more than applesauce or apple juice.
    - Adding naturally occurring levels of fiber to juice did not enhance satiety
- Houchins et al 2012
    - Effects of fruit and vegetable, consumed in solid vs beverage forms.
    - 21-week, randomized, crossover study
    - Participants consumed significantly less of a challenge meal after the ingestion of a solid fruit preload, compared to a beverage
    - Total daily energy intake was higher with the beverage fruit preload compared with the solid

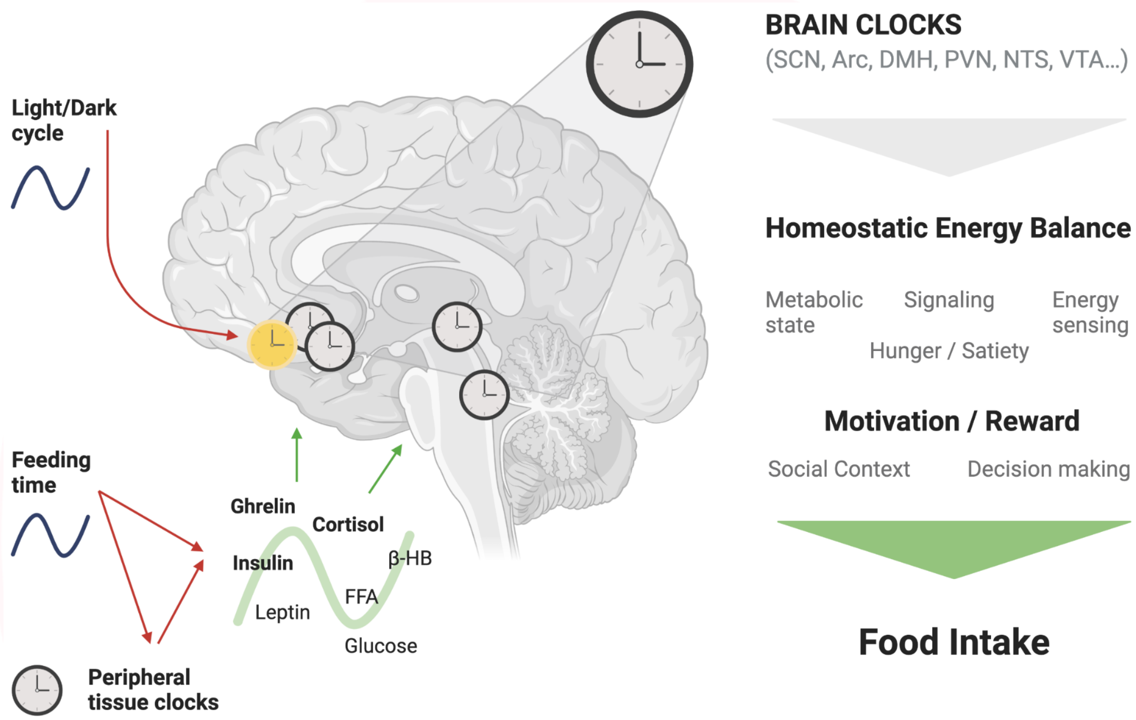


From: (Flood-Obbagy & Rolls, 2009)

- However, 'liquid vs solid' shouldn't be considered in isolation. Important to consider calorie density, fiber content, etc.
    - For example, studies show soups to be highly satiating.

Time of Day & Circadian Effects

- Both human and animal studies demonstrate time-of-day and circadian rhythmicity in reward and motivational responses (DePoy et al., 2017; Murray et al., 2002).
- Koch et al. (2020) demonstrated a role for the VTA in modulating rhythms in hedonic appetite regulation and sensitivity to hyper-palatable food overconsumption.



From: Flanagan et al., 2020

- Evidence that **front-loaded energy** (high-protein/high-carb breakfast) suppresses ghrelin during hypocaloric dieting, and that ghrelin remains suppressed into the post-weight loss period (Jakubowicz et al., 2012).
- Circadian rhythm in subjective hunger peaks at ~7 pm clock time (Scheer et al., 2013).
- **"Satiety ratio"** assesses how long an individual waits to eat again relative to the energy content of the prior eating occasion
  - It has been shown that the satiety ratio is highest in the morning and declines steadily over the course of the day (de Castro, 2004).
  - Thus, although more food may be consumed at an eating occasion later in the day, people may eat again sooner after that meal as a reflection of lower satiety.

- 'Big Breakfast Study' recently showed no difference between the **temporal distribution** of energy with regard to weight loss or energy expenditure but did find that high-energy morning intake was associated with significantly decreased subjective hunger and appetite (Ruddick-Collins et al., 2022).

Summary of Dietary Effects

1. Protein typically has a greater effect on satiety than other macronutrients.
2. Fat invokes a satiety response, but in typical food compositions, it is associated with high energy density and palatability, so it is readily over-consumed, leading to higher energy intakes.
3. Some types of fiber can promote satiety, but this highly depends on the type of fiber.
    a. Viscous fibers, such as pectin, appear to be the most satiating.
4. Lower-energy density foods appear to be more satiating than higher-energy density foods.

Note: As summarised excellently by Benelam (2009), *"Studying the effects of specific variables within a food or drink, without affecting others, is inherently difficult, and, when considering the results from studies on the effects of foods and drinks on satiety, it is important to consider any confounding factors that could have had an effect."*