ALINEA
NUTRITION

www.alineanutrition.com

OCTOBER 2022

TABLE OF CONTENTS

Buckland NJ, Camidge D, Croden F, et al. Women with a low-satiety phenotype show impaired appetite control and greater resistance to weight loss. *British Journal of Nutrition*. 2019;122(8):951-959.

What We Know, Think We Know, or Are Starting to Know

We are always going to have voices arguing that a single, isolated component of diet [see: sugar, seed oils] is "responsible" for increasing levels of bodyweight in the population. However, the reality is that the primary driver is an environment with constant availability of energy excess [1,2]. And this is not ideal for us *Sapiens*, a species that evolved to be very sensitive to the food environment [3,4].

It is plausible that the availability of energy-dense foods during human evolution was scarce and infrequent [3]. This scarcity of highly digestible foods in the natural environments of human evolution may have driven adaptations toward the ability to consume food beyond daily energy requirements, most likely for future energy storage [3].

Fast forward to the modern environment, and we can add environmental factors such as portion size, visibility, and availability, to the mix of factors that can trigger eating as an automatic behaviour, occurring without awareness or control over the eating episode [5].

All of this leads us to the complex neurobiology of regulating food intake in humans [6]. There are two overlapping processes that we must consider: satiation and satiety. *Satiation* can be thought of as 'intra-meal, i.e., the effects of food intake on internal inhibitory processes *during* consumption which bring the eating episode to an end [7,8]. *Satiety* can be thought of as 'post-ingestive, i.e., the effect *after* a meal on inhibitory mechanisms that influence subsequent appetite and return to hunger [7,8].

These inhibitory mechanisms of intra-meal and post-ingestive processes include [7–9]:

- Gastrointestinal and physical effects [e.g., food volume and rate of gastric emptying].
- Appetite-stimulating [known as 'orexigenic'] and appetite suppressing [known as 'anorexigenic'] pathways in the brain.
- Motivation-reward brain regions [for more detail on this, see ***Geek Box**, below].
- Psychosocial factors like mood and emotional state, social situations, and time of day.

Overconsumption of food arises when there is an imbalance between the biological drive to eat and these inhibitory processes [6,7].

What if people may have weaker satiety responses compared to others? In 2015, John Blundell's research group at the University of Leeds identified a "low-satiety phenotype", describing individuals with a behavioural susceptibility to overeat that reflected impaired satiety mechanisms [10].

The study we Deepdive into now is the most recent study from this group in women with a low-satiety phenotype.

*Geek Box: Homeostatic and Hedonic Regulation of Appetite

When we discuss concepts like satiation and satiety, it is important to note that these concepts are part of the overall framework of human appetite regulation. Appetite may be considered the set of processes that influence food intake; hunger reflects the motivational drive to eat food. As such, there are distinct processes that influence both appetite and hunger; these can be distinguished as homeostatic and hedonic processes. Homeostatic processes reflect the control over how much food is eaten, quantitatively [i.e., energy intake]. Homeostatic regulation of energy intake is a balance between orexigenic [i.e., appetite promoting] and anorexigenic [i.e., appetite suppressing] pathways in the brain, which influence both acute and long-term energy availability [both in diet and in stored energy, i.e., body fat]. In theory, eating behaviour would be governed solely by our energy requirements, where we would only consume as much energy as required to meet energy expenditure demands. However, humans evolved in natural environments with unpredictable food availability, and energy intake is not solely governed by homeostasis, with food-related motivation-reward processes and environmental factors influencing how much is eaten. The motivation-reward influence on eating is known as the hedonic process, driven by two sides to our brain reward systems: 'wanting', driven by dopamine, and 'liking', driven by opioids and cannabinoids. 'Wanting' triggers the intense motivational urge for the food reward, while the opioid-driven 'liking' response conveys the hedonic properties of food [often energy-dense, sugar, fat, and salt-rich foods]. The main point to take home is that homeostatic regulation of appetite is not tightly controlled, and hedonic motivation to eat is influenced by social, environmental, and cognitive factors, which can promote consuming energy in excess of homeostatic needs.

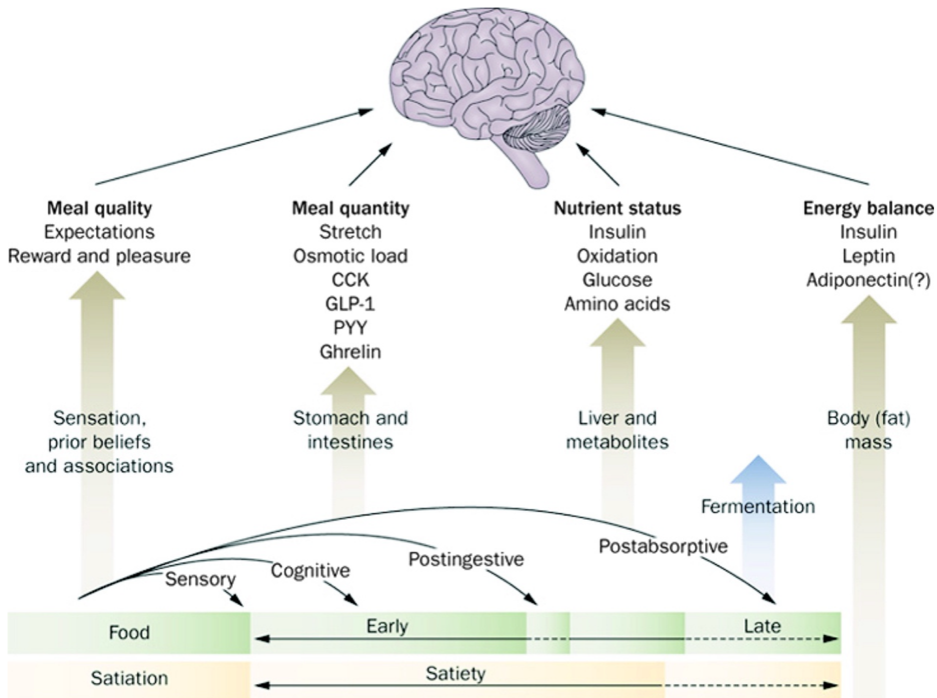

***Figure** from [7] illustrating the combination of factors influencing satiation and satiety in humans. As you can see from the graph, numerous biological, physiological, psychological, and environmental factors influence food intake [green **bar on bottom**] and both satiation and satiety [yellow **bar on bottom**]. Sensory and cognitive processes influence early food intake, before satiation induces an end to the meal; the post-ingestive and post-absorptive phase influences satiety, and how long may pass before a return to hunger and increased appetite again.*

The Study

This study was a secondary analysis of a randomised controlled trial that compared two weight management program diets in women with overweight/obesity:

- **Slimming World**: *Ad libitum* [Latin for "as much as desired"] intake of low energy-density foods.
- **NHS Live Well**: A 600kcal per day energy deficit with UK healthy eating guidelines.

Participants underwent a 2-week run-in to assess compliance before starting the diets, which were followed for 12-weeks. Participants completed subjective assessments of appetite and control of eating every week.

During the beginning and again at the end of the intervention, all participants underwent a test day in a laboratory that compared the effects of meals with different energy-density:

- Low energy-density meals of <0.8kcal per gram of food ['LED']
- High energy-density meals of >2.5kcal per gram of food ['HED']

These respective energy-densities were consumed at breakfast, lunch, dinner, and an evening snack. Meals were served 4 h apart. The test days compared the effects of the LED vs. HED meals on energy intake, appetite, and control of eating in a controlled, laboratory setting. Each participant completed both LED and HED test days, at both beginning and end of the study [see ***figure***, below].

To test this, both the evening meal and snack were *ad libitum*; participants were free to consume as much as desired, and energy intake was recorded to compare the LED and HED conditions. Breakfast and lunch provided 50% of total daily energy requirements.

The study divided participants into a "high satiety phenotype" ['HSP'] or "low satiety phenotype" ['LSP'], based on their subjective fullness scores in response to breakfast on the test days. The study analysed whether the "satiety phenotype" of participants influenced weight loss during the intervention, energy intake, food preferences, and appetite during the LED vs. HED test meal days.

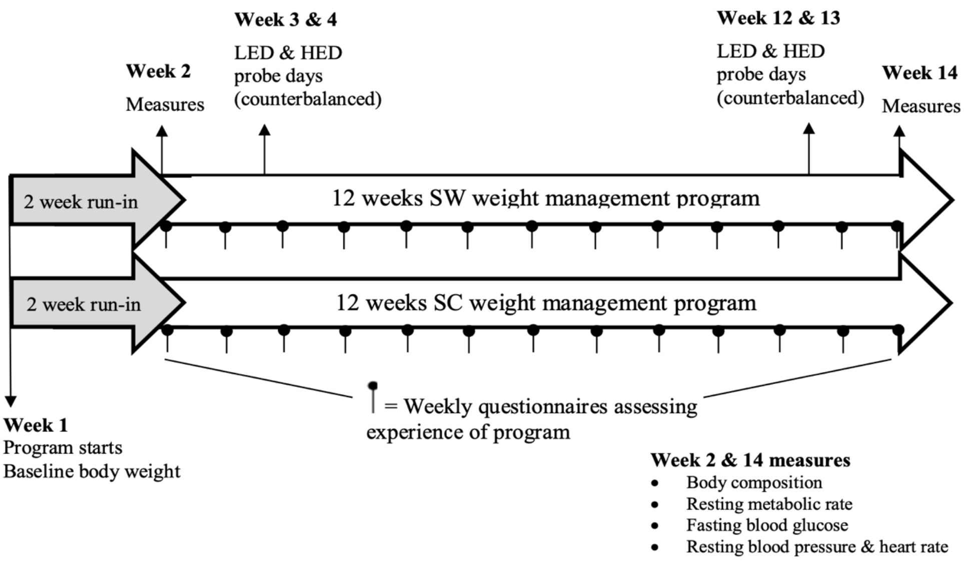

Figure *from the paper illustrating the study design. You can see that the 'probe' [test] days occurred at Weeks 3 and 4, and again at Weeks 12 and 13.*

Results: 96 women began the trial, of which 79 completed the full study. The average age and BMI were 41yrs and 34kg/m^2, respectively. 26 participants were classified as LSP and HSP, respectively. A further 27 participants were neither LSP or HSP and were not included in the analysis.

- ***Weight Loss During Weight Management Diets*:** The LSP lost 2.97kg [95% CI, 1.76kg to 4.17kg] over 12-weeks of the weight management diets, while the HSP lost 5.28kg [95% CI, 3.76kg to 6.80kg]. Fat mass [kg] was also greater in the HSP participants [see ***figure***, below].

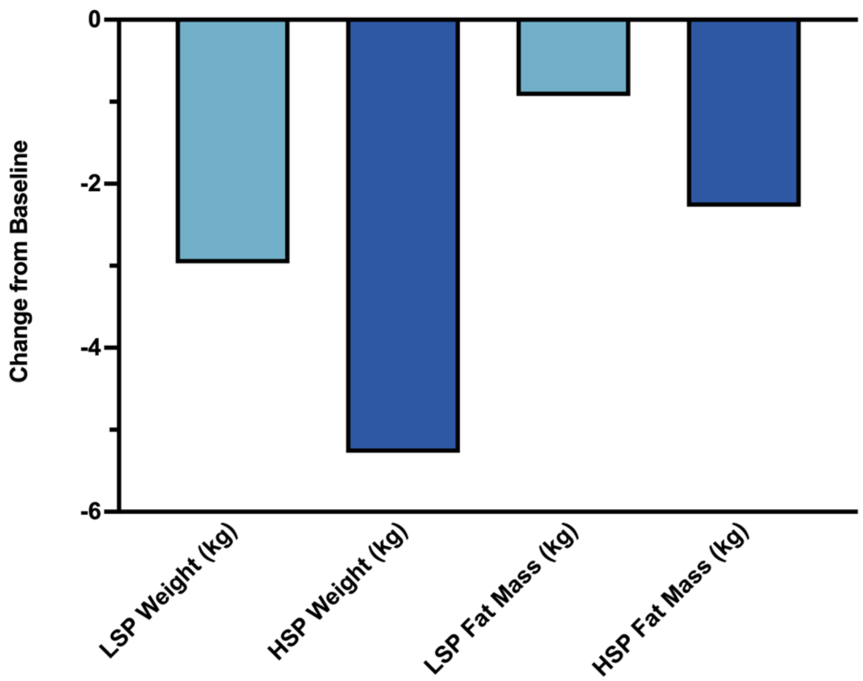

Figure *showing weight loss and fat mass loss in participants with a low-satiety phenotype [**LSP; sky blue bars**] and high-satiety phenotype [**HSP; royal blue bars**].*

- ***Appetite Control During Weight Management Diets*:** Compared to the HSP, the LSP participants found it harder to adhere to their diet, felt less able to stick to food choices, and reported significantly less control over their eating [see ***figure***, below].

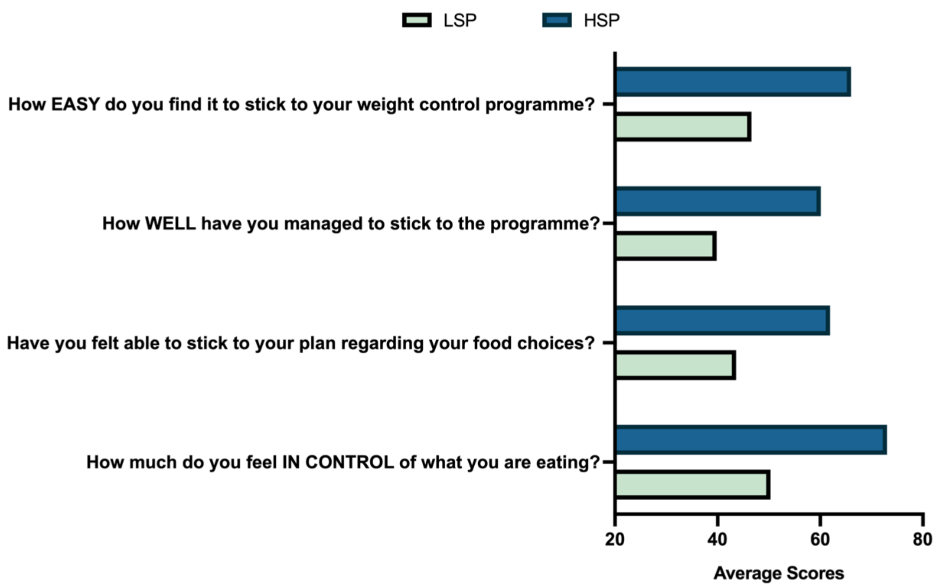

Figure *illustrating difference between LSP [**green bars**] and HSP [**blue bars**] on appetite control.*

- ***Food Intake and Food Preferences*:** Total daily energy intake was similar between LSP and HSP, during both the LED and HED test meal days. Energy intake at dinner was also similar. However, during the HED test days the LSP consumed 289kcal more energy intake with their evening snack compared to the HSP [see ***figure***, below]. The LSP participants showed higher 'liking' and 'wanting' responses to HED foods [more under ***Interesting Finding***, below].

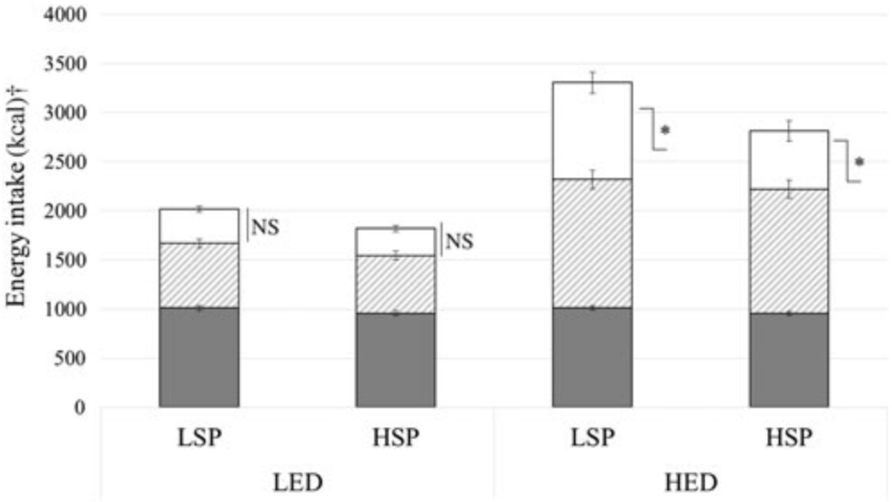

Figure *from the paper illustrating the differences between the LSP and HSP participants in response to the LED and HED test meal days. As you can see from the grey bold bar section, the breakfast and lunches provided the same amount of energy at 50% daily energy requirements. The dashed line bar section and white bold bar section represent the ad libitum dinner and snacks, respectively. 'NS' stands for 'not significant', i.e., energy intake overall and at each meal was similar between the LSP and HSP.*

The Critical Breakdown

Pros: The trial was preregistered at ClinicalTrials.gov, and the aims, hypotheses, and intended outcomes were all clearly stated in the preregistration. The test days used a counterbalance design, i.e., the order of testing for participants goes both ways [LED>HED and HED>LED], to minimise any effects of treatment order on outcomes. The analysis for weight loss outcomes used the intention-to-treat principle, where data from all participants is included irrespective of whether they completed the study, by using the last measurement available; this maintains balance between groups and minimises bias from imbalanced completion rates. Similar food products were used for both LED and HED test meals, differing in their energy density [e.g., low-fat product versions]. The study used validated assessments of hunger, appetite, and food preferences.

Cons: The main limitation to bear in mind is that the present study was a secondary analysis, also known as a 'post hoc' [Latin for 'after the event'] analysis. A secondary analysis is therefore an analysis which is undertaken after the main trial has concluded, using data from that trial, to look at a question that was not pre-registered. Because it is a secondary analysis and not part of the pre-planned study, it is important to note that a secondary analysis is an observational study, and can demonstrate associations, not cause-effect. The trial was non-randomised, and participants were already on the respective weight management programs, which also may have introduced selection bias. The sample size was small, and may have lacked statistical power to detect differences between groups.

Key Characteristic

Given what we know about appetite, the design of this trial is an important characteristic of the study; by combining both a 12-week intervention period with weekly appetite assessments and the acute test days, the study captured both short-term and longer-term appetite regulation processes.

This allowed the study to compare the short-term differences between satiety phenotypes in response to both low and high energy density meals, while also comparing whether the satiety phenotypes influenced weight loss and longer-term appetite outcomes over 12-weeks.

And what emerges from the data in this study suggests that the reason that the LSP participants had less success during the weight loss intervention may have been due to struggling with appetite control. We can see in the data from the weekly appetite assessments that LSP participants had significantly less control of eating episodes, struggled with food choices, and had difficulty following the prescribed diet.

And while the weekly appetite assessment relied on subjective measures, the laboratory test days used objective measurements of energy intake to allow for some insight into the potential impacts of lower appetite regulation. Which leads us to the next section…

Interesting Finding

What is really interesting is that it appears that the energy-density of foods interacts with the satiety phenotype to influence energy intake. In the test days, there was no difference between satiety phenotypes once LED foods were consumed. Thus, it is possible that even in the context of low satiety, LED foods may exert some benefit for appetite control.

However, the significant interaction between HED foods and the LSP is even more interesting because the significant differences emerged with evening snacking. This is interesting because even independent of satiety phenotypes, satiety is known to decrease across the day, correlating with greater energy intake in the evening [11].

Thus, the fact that the LSP consumed greater energy intake from HED foods in the evening suggests an interaction between the physical and sensory properties of the foods themselves [which were not observed with LED foods], and the behavioural influence of time-of-day.

Relevance

Is all lost for individuals with low satiety responsiveness? Perhaps not. The data from the present study, although a secondary analysis, suggests an effect of energy-density on appetite control. However, another randomised controlled trial tested the effects of an *ad libitum* low energy-density diet compared to a control diet in both low and high satiety phenotype men with obesity [(12)]. Although HSP men lost more weight overall, those on the LED diet showed greater weight loss compared to the control diet irrespective of satiety phenotype. Importantly, appetite control was significantly improved on the LED diet in both LSP and HSP participants.

A recent meta-analysis of 12 interventions targeting satiety enhancement in diets showed that enhancing satiety and improving appetite control resulted in an average of 3.60kg [95% CI, 1.05kg to 6.15kg] greater weight loss compared to control diets [(13)]. This is consistent with research demonstrating that reductions in appetite correlate with improved weight management, both acutely and sustained over 12-weeks [(14)].

It is important to note that emotive and behavioural aspects of appetite are distinct, and one cannot simply be considered a proxy for the other [(15)]. This is crucial when we consider appetite regulation because it is possible to target specific dietary behaviours that may enhance appetite regulation. For example, Jakubowicz *et al*. [(16)] showed that consuming high-energy breakfasts that emphasised protein and carbohydrate intake lead to significant suppression of ghrelin, the 'hunger hormone', an effect that persisted up to 16-weeks after the initial weight loss intervention.

The effect of high morning energy intake on appetite was recently confirmed in a more rigorously controlled intervention, which showed that consuming ~40% energy at breakfast led to significant reductions in subjective appetite over the course of the day, compared to the same amount of energy at dinner [(17)].

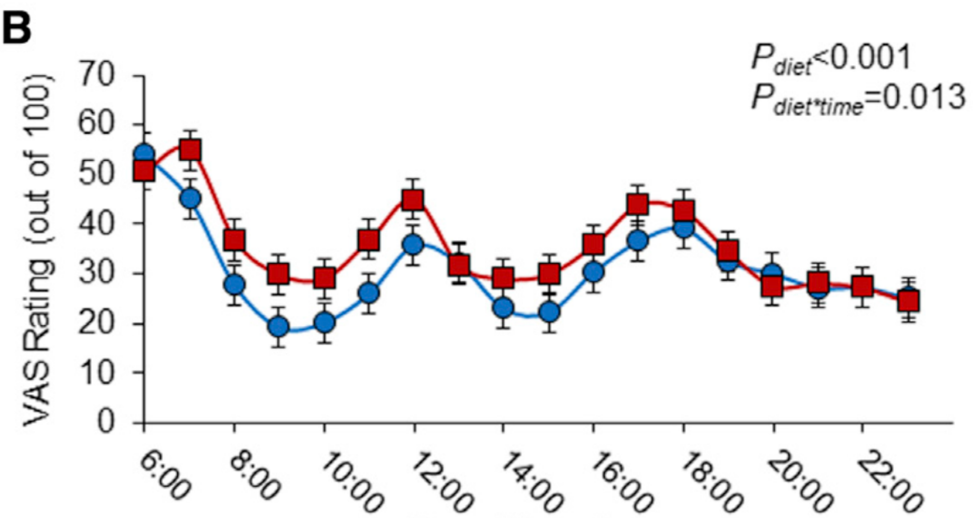

Figure *from* [(17)] *illustrating the effects of high morning energy intake [**blue line**] compared to high evening energy intake [**red line**] on appetite ratings over the course of the day.*

Thus, it is plausible that while humans with low satiety responsiveness may be biologically predisposed to overconsume when highly palatable, energy-dense foods are available, there are also strategies that are available to mitigate this through enhancing satiety and appetite.

Application to Practice

While at first glance these findings may appear to be disheartening for people who struggle with appetite control, in fact from an application perspective this may not be the case. The findings in relation to the effects of LED foods, and in terms of what we know about the wider impact of time-of-day on appetite control, indicate that there are ways of enhancing the satiety derived from diet, while improving appetite.

The first appears to be an emphasis on enhancing satiety through diet; high volume, low energy-density foods [non-starchy vegetables, fruits, legumes, Greek yogurt, etc.] appear to benefit appetite control and satiety in individuals with a low-satiety phenotype (12). A second strategy would be to front-load energy intake, aiming for high energy intakes early in the day, which appears to enhance appetite regulation, suppress ghrelin, and attenuate evening hunger levels (11,16,17).

References

1. Swinburn BA, Sacks G, Lo SK, Westerterp KR, Rush EC, Rosenbaum M, et al. Estimating the changes in energy flux that characterize the rise in obesity prevalence. Am J Clin Nutr. 2009 Jun 1;89(6):1723–8.

2. Swinburn B, Sacks G, Ravussin E. Increased food energy supply is more than sufficient to explain the US epidemic of obesity. Am J Clin Nutr. 2009 Dec 1;90(6):1453–6.

3. Milton K. Hunter-gatherer diets—a different perspective. Am J Clin Nutr. 2000 Mar 1;71(3):665–7.

4. Lowe MR. Self-Regulation of Energy Intake in the Prevention and Treatment of Obesity: Is It Feasible? Obes Res. 2003 Oct;11(S10):44S-59S.

5. de Castro JM. Socio-cultural determinants of meal size and frequency. British Journal of Nutrition. 1997 Apr 9;77(S1):S39–55.

6. Casanova N, Finlayson G, Blundell JE, Hopkins M. Biopsychology of human appetite — understanding the excitatory and inhibitory mechanisms of homeostatic control. Curr Opin Physiol. 2019 Dec;12:33–8.

7. Tremblay A, Bellisle F. Nutrients, satiety, and control of energy intake. Applied Physiology, Nutrition, and Metabolism. 2015 Oct;40(10):971–9.

8. Benelam B. Satiation, satiety and their effects on eating behaviour. Nutr Bull. 2009 Jun;34(2):126–73.

9. de Castro JM. The control of food intake of free-living humans: Putting the pieces back together. Physiol Behav. 2010 Jul;100(5):446–53.

10. Dalton M, Hollingworth S, Blundell J, Finlayson G. Weak Satiety Responsiveness Is a Reliable Trait Associated with Hedonic Risk Factors for Overeating among Women. Nutrients. 2015 Sep 4;7(9):7421–36.

11. de Castro JM. The Time of Day of Food Intake Influences Overall Intake in Humans. J Nutr. 2004;134(1):104–11.

12. Arguin H, Tremblay A, Blundell JE, Després JP, Richard D, Lamarche B, et al. Impact of a non-restrictive satiating diet on anthropometrics, satiety responsiveness and eating behaviour traits in obese men displaying a high or a low satiety phenotype. Br J Nutr. 2017 Nov 14;118(9):750–60.

13. Hansen TT, Andersen SV, Astrup A, Blundell J, Sjödin A. Is reducing appetite beneficial for body weight management in the context of overweight and obesity? A systematic review and meta - analysis from clinical trials assessing body weight management after exposure to satiety enhancing and/or hunger reducing products. Obesity Reviews. 2019 Jul 3;20(7):983–97.

14. Hansen TT, Mead BR, García-Gavilán JF, Korndal SK, Harrold JA, Camacho-Barcía L, et al. Is reduction in appetite beneficial for body weight management in the context of overweight and obesity? Yes, according to the SATIN (Satiety Innovation) study. J Nutr Sci. 2019 Nov 27;8:e39.

15. Holt GM, Owen LJ, Till S, Cheng Y, Grant VA, Harden CJ, et al. Systematic literature review shows that appetite rating does not predict energy intake. Crit Rev Food Sci Nutr. 2017 Nov 2;57(16):3577–82.

References

16. Jakubowicz D, Froy O, Wainstein J, Boaz M. Meal timing and composition influence ghrelin levels, appetite scores and weight loss maintenance in overweight and obese adults. Steroids. 2012;77(4):323–31.

17. Ruddick-Collins LC, Morgan PJ, Fyfe CL, Filipe JAN, Horgan GW, Westerterp KR, et al. Timing of daily calorie loading affects appetite and hunger responses without changes in energy metabolism in healthy subjects with obesity. Cell Metab. 2022 Sep 4;34:1-14.