From dearth to excess: The rise of obesity in an ultra-processed food system

Kevin D. Hall, Ph.D.

Integrative Physiology Section Chief; Laboratory of Biological Modeling; National Institute of Diabetes & Digestive & Kidney Diseases; National Institutes of Health; 12A South Drive, Room 4007; Bethesda, MD 20892-4007

* Correspondence: kevin.hall@nih.gov

Abstract: More people around the world now have obesity than suffer from starvation thanks to our modern food system. Agriculture was transformed over the 20th century by a variety of technological advancements that relied heavily on fossil fuels. In the United States of America, government policies and economic incentives led to surplus production of cheap inputs to processed food industries that produced a wide variety of heavily marketed, convenient, rewarding, timesaving, and relatively inexpensive ultra-processed foods. The energy available in the United States food supply increased much more than population needs, albeit with large inequities in food distribution and nutrition security. While most of the rise in per capita food availability during the late 20th and early 21st centuries in the United States resulted in increased food waste, a variety of mechanisms have been proposed by which changes in the increasingly ultra-processed food environment resulted in excess energy intake disproportionately in people genetically susceptible to obesity. As populations continue to grow, substantial investments in coordinated nutrition and agricultural research are needed to transform our current food system to one that relies less on fossil fuels, preserves biodiversity, ensures environmental health, and provides equitable access to affordable, safe, and nutritious food that reduces the prevalence of chronic diseases like obesity.

Keywords: Obesity; food system; agriculture; ultra-processed food

---

Introduction

Producing enough food has challenged humans for millennia. The 18th century English economist Thomas Malthus made dire predictions that population growth will outpace agriculture's ability to provide sufficient food thereby resulting in mass starvation [1]. Echoes of what has become known as the 'Malthusian trap' have reverberated for centuries since. For example, in the late 1960s and early 1970s the American biologist Paul Ehrlich predicted in that the United States of America (USA) would experience famines killing millions of mass starvation by the middle of the 1980s [2] – a period that was instead marked by a troubling increase in obesity prevalence [3]. Indeed, more people around the world now have obesity than suffer from hunger [4]. How did this happen? Here, I sketch how the development of the current industrialized food system has thus far avoided the Malthusian trap and instead may have caused the increase in obesity prevalence. For purposes of concision, this brief review will focus on the USA, but food systems are now multinational and parallels exist in other industrialized nations with important implications for emerging markets.

The rise of the industrialized food system

Agriculture has relied on hard physical work of humans and draft animals for millennia. In the 18th century, seed drills mechanized planting and steel plows were introduced the 19th century, but it wasn't until the 20th century when agriculture was transformed by machines powered by fossil fuels replacing the vast majority of muscular farm work [5-8]. Mass mechanization of farming dramatically improved efficiency and more land could be farmed by fewer farm workers and without the need to also produce feed for draft animals.

Fossil fuels also transformed agriculture by indirectly increasing fertility of the soil. Specifically, soil nitrogen content sets a limit on the rate of protein synthesis and plant growth because nitrogen is an essential component of all amino acids. Atmospheric nitrogen is naturally fixed in the soil by bacteria that synthesize ammonia which is readily absorbed by plants, but increasing plant growth could be achieved by supplementing soil nitrogen with application of manure and guano. Unfortunately, the availability of sufficient natural fertilizers posed a limitation that was eliminated in the early 20th century when German chemists Fritz Haber and Carl Bosch invented a way to artificially synthesize ammonia from atmospheric nitrogen at industrial scale. Unfortunately, the Haber-Bosch process traditionally uses a substantial amount of fossil fuel [7, 8].

Twentieth century expansion of agricultural productivity and markets in the USA was facilitated by public investments in infrastructure, especially irrigation and transportation networks. Agricultural research resulted in the development of hybrid seeds for grains like corn, wheat, and soybeans that capitalized on the improved irrigation and fertilization of the soil to dramatically increase crop yields and select for varieties amenable to efficient mechanized harvesting. An industrial chemical revolution also produced new classes of pesticides, fungicides, and herbicides to further increase productivity [5-9].

These technological advancements have been collectively called the "Green Revolution" and are credited for avoiding the dire Malthusian predictions. In past several decades, advancements in molecular biology have resulted in the introduction of genetically modified organisms to agriculture in the hopes of further increasing productivity and improving nutritional quality of certain crops.

The grain commodity crops that have most benefited from the "Green Revolution" provided more than enough protein and calories to feed the growing population without substantial increases in land use. But food is more than protein and calories and the vast majority of commodity crops are not directly consumed by humans. Rather, most are used as feed for cows, pigs, and chickens that are subsequently consumed by humans. Animal agriculture became increasingly dependent on grains, antibiotics, and confined feedlots to increase the growth efficiency of animals and bring them to market sooner. Furthermore, such practices allowed the animals to be located nearby slaughterhouses and transportation networks facilitated their efficient delivery to market [5, 6].

Government policies in the USA have incentivized farm specialization, increased commodity crop production, and promoted larger farm sizes. Indeed, the number of farms and people working on farms has decreased substantially over the past several decades, and draft animals are now practically nonexistent [6]. As a result, much of the rural population moved to cities and suburbs whose residents rely on others to produce their food.

Improvements in transportation networks, manufacturing methods, food packaging and preservation technologies enabled the rise of large national and multi-national food brands. These processed food and beverage manufactures relied on inexpensive agricultural inputs of protein and calories and their food scientists invented ingenious processing methods to "add value" to their products [9]. Products were fortified with vitamins and minerals, flavors were enhanced with additives, textures were engineered to improve "mouth feel", and other technologies were applied to increase the overall appeal of their products that were sold for a considerable profit [10, 11].

Processed food companies grew at an astonishing rate in the 20th century. Investments in research and development resulted in an ever-expanding range of new products that were more convenient, time-saving, and tasty. Intense competition in the marketplace resulted in a "survival of the fittest" products along with directed evolution of new products that were iteratively more and more successful. When a sufficient market of consumers objected to certain products on offer, industry responded by offering a new line of "gluten free", "low fat", "low carb", or other products in addition to the existing products thereby capturing additional market share.

Food and beverage industries have a guaranteed market because we all need to eat. However, these industries are faced with a fundamental limitation when it comes to their growth: Engel's law states that a person's spending on food decreases as a percentage of their increasing income, in part, because food requirements are physiologically limited. Thus, even in a growing economy, profit growth of food and beverage companies is reliant on increasing the size of their market to a greater extent than other industries. Shareholders of individual food and beverage companies demand increased profits which incentivizes aggressive marketing campaigns to replace traditional foods and incentivizes development of a wide variety products that can be easily consumed above physiological needs. Increasing portion sizes appeal to the consumer's sense of value for money and promotion of snacking behavior alters social norms of eating and further increases opportunities for consumption [12].

Beyond increasing food and beverage consumption in existing markets, another way for processed food companies to increase profits is to enter new markets and displace traditional foods. For example, in 2010 the world's largest food manufacturer Nestlé issued a press release announcing the launch of a "floating supermarket" stocked with Nestlé products on the Amazon River touting the project as an "Unprecedented Business Model [that] will extend the company's presence in Brazilian households" [13].

Ultra-processed foods

Even before the launch of Nestlé's "floating supermarket", Carlos Monteiro documented an alarming increase in industrially processed food products entering the Brazilian market and displacing more traditional foods [14]. To better document and measure this shift in the food supply, in 2010 Monteiro introduced a new food categorization system called NOVA that classified foods based on the extent and purpose of processing [14]. Originally containing only three categories [14], the NOVA system was later modified to include four categories [15] . Unprocessed or minimally processed foods such as whole foods that have been washed, chopped, frozen, dried, or fermented; 2. Processed culinary ingredients such as sugar, butter, cooking oils, and salt; 3. Processed foods that are combinations of category 1 and 2 foods for purposes of preservation or to increase palatability; and 4. Ultra-processed foods whose definition has been the subject of some debate and confusion prompting clarifications [16]. The most recent definition of ultra-processed foods is that they are "industrial formulations manufactured by deconstructing foods into their component parts, modifying them and recombining them with a myriad of additives and little, if any, whole foods. Importantly, ultra-processed foods are distinct not only in terms of their ingredient composition, but also in terms of the purpose for which they are produced. The purpose underlying the manufacture of ultra-processed foods is to create convenient (durable, ready-to-consume), tasteful (often hyper-palatable) and highly profitable (cheap ingredients, value adding) products that are liable to displace all other NOVA food groups" [17].

Food and nutrition professionals have expressed confusion about the concept of ultra-processed food which is often conflated with "processed food" [18] thereby ignoring the "purpose of processing" criterion as an important part of the NOVA category 4 definition. While producers of all NOVA food categories intend to generate profits, ultra-processed foods have a uniquely wide scope for extensive reformulation to meet market demands and potentially displace consumption of foods from other categories. Thus, some have argued that ultra-processed foods would be better described as "ultra-formulated" foods [19].

The NOVA food classification system has been met with substantial criticism [20-27]. Some critics have argued that the NOVA system is unclearly defined and difficult to implement, with substantial discrepancies between different people asked to rate the same foods according to the NOVA system [28]. However, other studies have found more consistent NOVA ratings between people [29] and standardized approaches to applying the NOVA system are being implemented [30].

Another criticism is that the NOVA system offers no meaningful benefits over traditional nutrient-based classification systems because diets high in ultra-processed foods also tend to have greater amounts of salt, sugar, and fat while being lower in protein and fiber [20]. However, the NOVA system largely ignores the nutrient content of foods and appears to reject the dominant "nutritionism" paradigm that the nutrient composition of foods is the main determinant of their impact on health [31] – an approach with long history of success in nutrition science [32]. Nevertheless, despite widespread use of "nutritionism" based approaches to communicating about healthy and unhealthy foods or dietary patterns, many consumers understand the basic advice to minimize ultra-processed food intake more easily than recommendations to reduce consumption of precisely defined nutrients such as sodium, saturated fat or sugar.

Official dietary guidelines of health organizations and nations have begun to include statements to limit consumption ultra-processed foods [33] because they have been linked to a variety of poor health outcomes, including obesity [34-36]. The processed food industry is especially concerned about widespread adoption of the NOVA system because reformulating products out of the NOVA 4 category will be very difficult if widespread recommendations to decrease consumption of ultra-processed food are heeded. Furthermore, the NOVA 4 definition currently represents such a wide variety of products that there is a risk of enacting ineffective and regressive policies without a better mechanistic understanding of how ultra-processed foods cause adverse health outcomes [37]. However, by subcategorizing NOVA category 4 foods based on a better understanding of biological mechanisms it may be possible to help reformulate ultra-processed foods and provide effective consumer advice on the basis of their individual risk of a disease or health condition such as obesity [37].

Increasing obesity prevalence and the changing food environment

Within a given food environment, individual susceptibility to obesity is largely explained by genetic differences, particularly genes preferentially expressed in the brain and likely involved in appetite control [38]. The changing food environment is thought to explain the increasing prevalence of obesity in the population [39], and our modern industrialized food system has provided excess calories in the form of increased availability and marketing of inexpensive and convenient ultra-processed foods.

There is much debate about the most important factors in our changing food environment that are responsible for the increase in obesity prevalence. Associations between ultra-processed food intake and obesity observed in epidemiological studies [34-36] do not necessarily imply that ultra-processed foods cause excess intake and weight gain. We recently conducted controlled randomized crossover trial to investigate this issue and found that a diet high in ultra-processed foods caused an increase in ad libitum energy intake of ~500 kcal/d and weight gain in adults as compared to an unprocessed diet matched for overall presented calories, carbohydrate, sugar, fat, sodium, energy density, glycemic load, and fiber that resulted in spontaneous weight loss [40]. There are a variety of mechanism that may have been responsible for these results.

Mechanisms by which ultra-processed foods promote excess energy intake and obesity

A wide variety of mechanisms have been proposed to explain why diets high in ultra-processed foods are consumed in caloric excess and may lead to obesity with varying degrees of plausibility [27, 33]. Many potentially important mechanisms involve cost, convenience, preparation time, availability, variety, and marketing that affect food choice and frequency of consumption. However, these mechanisms were not at play in our randomized trial because participants were freely provided with all their meals and snacks ready to consume. Below, I will focus mainly on the mechanisms that could have played a role in our study.

One highly plausible mechanism by which ultra-processed foods may promote obesity involves their typically high energy density which is a property that is well-known to positively affect ad libitum energy intake [41]. While the overall energy densities of the ultra-processed and minimally processed diets in our study were matched, this was achieved primarily by including more low-calorie beverages with the ultra-processed meals to deliver soluble fiber supplements to match the overall fiber content of the minimally processed diet [40]. Non-beverage energy density differed substantially between the ultra-processed and minimally processed diets, primarily because of decreased water content in the ultra-processed foods. In a secondary analysis of the meal intake data, non-beverage energy density was an important variable positively predicting meal energy intake and mediating a substantial fraction of the effect of ultra-processed versus minimally processed meal energy intake in our trial [42].

Eating rate has been implicated as a mechanism that positively promotes energy intake and is related to the sensory properties and structure of the foods [43-45]. Ultra-processed meals in our study were consumed more quickly than the minimally processed meals when including the masses of the beverages but non-beverage items in the ultra-processed meals were eaten more slowly than in the minimally processed meals [42]. In a secondary analysis, non-beverage eating rate was a positive predictor of individual meal energy intake [42].

While the overall diets were matched each day for sodium, sugar, carbohydrates, and fat in our trial, the individual meals differed in the proportion of calories presented as hyper-palatable foods defined as having high amounts of both sodium and fat, sodium and carbohydrates, and sugar and fat [46]. Indeed, neuroimaging studies have suggested that hyperpalatable foods high in sugar and fat are particularly reinforcing [47]. In a secondary analysis of our ultra-processed versus minimally processed diet study, we found that meal energy intake was positively influenced by hyper-palatable foods as a proportion of calories presented [42]. We also found an interesting interaction between non-beverage meal energy density and hyper-palatable foods such that the effect of hyper-palatable foods was greater for meals with lower energy density and vice versa.

Interestingly, the participants in our trial did not report significant differences in palatability between the ultra-processed versus minimally processed meals [40]. However, palatability is only a single dimension of the multifaceted concept of food reward [48] and ultra-processed meals may have increased incentive salience, wanting, and motivation to eat that may have driven excess energy intake [49].

Some investigators have hypothesized that ultra-processed foods contain highly processed carbohydrates that are quickly absorbed causing rapid increases in circulating glucose thereby enhancing reward related brain activity via mechanisms similar addictive substances [50, 51]. The subsequent fall in in circulating glucose may also result in late-postprandial glucose dips that induce hunger [52]. While the ultra-processed and minimally processed diets used in our trial varied in added sugars, the diets were similar in glycemic load and resulted in no significant differences in mean glucose or glucose variability as measured using continuous glucose monitors [40, 53].

Ultra-processed foods tend to have lower protein content [54] and the protein leverage model of obesity suggests that diets with diluted dietary protein result in excess energy intake to achieve a given protein target [55, 56]. While our ultra-processed and minimally processed diets differed slightly in the proportion of presented calories as protein (14% versus 15.6%, respectively) we calculated that protein leverage could not fully explain the observed differences in mean energy intake [40, 57]. Indeed, in a secondary analysis of our ultra-processed and minimally processed meal data we found that more protein offered with meals significantly increased energy intake [42].

A variety of gut signals are modulated in response to food ingestion and are believed to play important roles in appetite control [58]. The production of ultra-processed foods disrupts the natural food matrix of the whole food ingredients and may result in altered intestinal digestion and absorption of nutrients [59]. For example, if nutrients from ultra-processed foods are absorbed more proximally in the gut they may instigate a different pattern of gut-brain signals as compared to the same nutrients ingested in the form of minimally processed whole foods. These gut-brain signals include vagal afferents, hormones derived from enteroendocrine cells, or signals from the intestinal microbiota. Enteroendocrine cells and microbiota may also be negatively influenced by low amounts of insoluble fiber or various emulsifiers or additives in ultra-processed foods. Another ingredient of ultra-processed food involves the materials used in packaging which may alter the endocrine system and act as obesogens [60, 61].

Another property of ultra-processed foods is that bioactive compounds that are found in whole foods are often removed and additives, such as artificial flavors, may have unintended biological activity. It has been proposed that the relative concentrations of nutrients, flavors, and bioactive compounds that were previously reliable over evolutionary time and were used to guide our food intake to meet physiological demands have become mismatched by the rise in ultra-processed foods and have resulted in aberrant food intake behavior promoting weight gain [49, 62]. For example, the increasing prevalence of ultra-processed foods in the food supply has gone along with an increase in fats derived from processed seed oils which have a high proportion of omega 6 to omega 3 unsaturated fatty acids that have been suggested to promote obesity through various mechanisms, including influencing the endocannabinoid system to increase appetite [63-65].

Conclusions

Through a variety of technological advancements, government policies, and economic incentives, the current food system in the USA relies heavily on fossil fuels to generate a huge surplus of calories available in a wide variety of heavily marketed foods that are inexpensive, convenient, ubiquitous, energy dense, and often hyperpalatable. This flow of matter and energy through the industrialized food system in the USA has increased over the past half century on a per capita basis in correspondence with the rise in obesity prevalence [3] and an even larger increase in food waste [66].

We find ourselves in a unique position in human history where food is produced in excess by relatively small numbers of people and is relatively affordable. Whereas food purchases represented ~60% of disposable income at the beginning of the 20th century in the USA, now, food costs <10% of disposable income [12]. The benefits of these changes include the fact that more food is prepared outside the home and cooking meals at home is more convenient thereby freeing up time and money for other pursuits.

It is intriguing to speculate that increasing obesity prevalence has been an inevitable result of striving to create a food system that avoids Malthus' predictions. In other words, society has incentivized surplus agricultural production (relying on cheap fossil fuels) to provide low-cost inputs to food and beverage industries that produce heavily marketed, convenient, rewarding, timesaving, and relatively inexpensive ultra-processed foods in great excess of consumption needs of the population, albeit with large inequities in food distribution and nutrition security [4].

We are now faced with a huge challenge and opportunity. As populations continue to grow and agriculture faces the added pressures of tackling climate change and loss of biodiversity, substantial investments in coordinated nutrition and agricultural research are urgently needed to transform our current food system to one that relies less on fossil fuels, ensures environmental health, and provides equitable access to affordable, safe, and nutritious food that reduces the prevalence of chronic diet-related diseases like obesity.

Acknowledgments: This work was supported by the Intramural Research Program of the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases.

References

[1] Malthus, T. R. 1798 *An Essay on the Principle of Population*. London.
[2] Ehrlich, P. R. & Ehrlich, A. H. 1968 *The Population Bomb*, Ballantine Books.
[3] Swinburn, B. A., Sacks, G., Hall, K. D., McPherson, K., Finegood, D. T., Moodie, M. L. & Gortmaker, S. L. 2011 The global obesity pandemic: shaped by global drivers and local environments. *Lancet* **378**, 804-814.

[4] FAO, I., UNICEF, WFP and WHO. 2019 The State of Food Security and Nutrition in the World 2019. Safeguarding against economic slowdowns and downturns. (Rome, Food and Agriculture Organization of the United Nations.
[5] Blaxter, K. L. & Robertson, N. 1995 *From Dearth to Plenty: The modernrevolution in food production*. Cambridge, England, Cambridge University Press.
[6] Gardner, B. L. 2002 *American Agriculture in the Twentieth Century: How it Flourished and What it Cost*. Cambridge, MA, Harvard University Press.
[7] Smil, V. 2000 *Feeding the world: A challenge for the twenty-first century*. Cambridge, The MIT Press.
[8] Smil, V. 2022 *How the World Really Works: The Science Behind How We Got Here and Where We're Going*. London, Viking.
[9] Roberts, P. 2008 *The end of food*. New York, Houghton Mifflin Harcourt Publishing Company; 400 p.
[10] Moss, M. 2013 *Salt, sugar, fat: how the food giants hooked us*. New York, Random House; 446 p.
[11] Schatzker, M. 2015 *The dorito effect: The surprising new truth about food and flavor*. New York, NY, Simon & Schuster; 259 p.
[12] Nestle, M. 2002 *Food Politics: How the Food Industry Influences Nutrition and Health*, University of California Press.
[13] Nestlé. 2010 NESTLÉ LAUNCHES FIRST FLOATING SUPERMARKET IN THE BRAZILIAN NORTH REGION: Unprecedented Business Model will service the riverside communities in the Amazon and will extend the company's presence in the Brazilian households. (
[14] Monteiro, C. A., Levy, R. B., Claro, R. M., Castro, I. R. & Cannon, G. 2010 A new classification of foods based on the extent and purpose of their processing. *Cadernos de saude publica* **26**, 2039-2049.
[15] Monteiro, C. A., Cannon, G., Levy, R. B., Moubarac, J. C., Jaime, P., Martins, A. P., Canella, D., Louzada, M. & Parra, D. 2016 NOVA. The star shines bright. *World Nutrition* **7**, 28-38.
[16] Monteiro, C. A., Cannon, G., Levy, R. B., Moubarac, J. C., Louzada, M. L., Rauber, F., Khandpur, N., Cediel, G., Neri, D., Martinez-Steele, E., et al. 2019 Ultra-processed foods: what they are and how to identify them. *Public Health Nutr* **22**, 936-941. (DOI:10.1017/s1368980018003762).
[17] Scrinis, G. & Monteiro, C. 2022 From ultra-processed foods to ultra-processed dietary patterns. *Nature Food* **3**, 671-673. (DOI:10.1038/s43016-022-00599-4).
[18] Sadler, C. R., Grassby, T., Hart, K., Raats, M. M., Sokolović, M. & Timotijevic, L. 2022 "Even We Are Confused": A Thematic Analysis of Professionals' Perceptions of Processed Foods and Challenges for Communication. *Front Nutr* **9**, 826162. (DOI:10.3389/fnut.2022.826162).
[19] Levine, A. S. & Ubbink, J. Ultra-processed foods: Processing versus formulation. *Obesity Science & Practice* **n/a**. (DOI:https://doi.org/10.1002/osp4.657).
[20] Astrup, A. & Monteiro, C. A. 2022 Does the concept of "ultra-processed foods" help inform dietary guidelines, beyond conventional classification systems? NO. *Am J Clin Nutr* **116**, 1482-1488. (DOI:10.1093/ajcn/nqac123).
[21] Drewnowski, A. 2022 Matters Arising: Food Compass novelty and NOVA category assignments. *Nature Food* **3**, 581-583. (DOI:10.1038/s43016-022-00556-1).
[22] Forde, C. G. 2023 Processing the evidence to evaluate mechanisms, costs and future solutions. *Nutr Bull*. (DOI:10.1111/nbu.12623).
[23] Gibney, M. J. 2022 Ultra-processed foods in public health nutrition: the unanswered questions. *Br J Nutr*, 1-4. (DOI:10.1017/s0007114522002793).
[24] Gibney, M. J. & Forde, C. G. 2022 Nutrition research challenges for processed food and health. *Nature Food* **3**, 104-109. (DOI:10.1038/s43016-021-00457-9).
[25] Gibney, M. J., Forde, C. G., Mullally, D. & Gibney, E. R. 2017 Ultra-processed foods in human health: a critical appraisal. *Am J Clin Nutr* **106**, 717-724. (DOI:10.3945/ajcn.117.160440).
[26] Lockyer, S., Spiro, A., Berry, S., He, J., Loth, S., Martinez-Inchausti, A., Mellor, D., Raats, M., Sokolović, M., Vijaykumar, S., et al. 2023 How do we differentiate not demonise - Is there a role for healthier processed foods in an age of food insecurity? Proceedings of a roundtable event. *Nutr Bull*. (DOI:10.1111/nbu.12617).
[27] Valicente, V. M., Peng, C. H., Pacheco, K. N., Lin, L., Kielb, E. I., Dawoodani, E., Abdollahi, A. & Mattes, R. D. 2023 Ultraprocessed Foods and Obesity Risk: A Critical Review of Reported Mechanisms. *Advances in nutrition (Bethesda, Md.)*. (DOI:10.1016/j.advnut.2023.04.006).
[28] Braesco, V., Souchon, I., Sauvant, P., Haurogné, T., Maillot, M., Féart, C. & Darmon, N. 2022 Ultra-processed foods: how functional is the NOVA system? *Eur J Clin Nutr* **76**, 1245-1253. (DOI:10.1038/s41430-022-01099-1).
[29] Sneed, N. M., Ukwuani, S., Sommer, E. C., Samuels, L. R., Truesdale, K. P., Matheson, D., Noerper, T. E., Barkin, S. L. & Heerman, W. J. 2023 Reliability and validity of assigning ultraprocessed food categories to 24-h dietary recall data. *Am J Clin Nutr* **117**, 182-190. (DOI:10.1016/j.ajcnut.2022.10.016).

[30] Steele, E. M., O'Connor, L. E., Juul, F., Khandpur, N., Galastri Baraldi, L., Monteiro, C. A., Parekh, N. & Herrick, K. A. 2023 Identifying and Estimating Ultraprocessed Food Intake in the US NHANES According to the Nova Classification System of Food Processing. *The Journal of Nutrition* **153**, 225-241. (DOI:https://doi.org/10.1016/j.tjnut.2022.09.001).
[31] Scrinis, G. 2013 *Nutritionism: The science and politics of dietary advice*. New York, Columbia University Press; 352 p.
[32] Mozaffarian, D., Rosenberg, I. & Uauy, R. 2018 History of modern nutrition science-implications for current research, dietary guidelines, and food policy. *Bmj* **361**, k2392. (DOI:10.1136/bmj.k2392).
[33] Monteiro, C. A. & Astrup, A. 2022 Does the concept of "ultra-processed foods" help inform dietary guidelines, beyond conventional classification systems? YES. *Am J Clin Nutr* **116**, 1476-1481. (DOI:10.1093/ajcn/nqac122).
[34] Juul, F., Vaidean, G. & Parekh, N. 2021 Ultra-processed Foods and Cardiovascular Diseases: Potential Mechanisms of Action. *Advances in nutrition (Bethesda, Md.)* **12**, 1673-1680. (DOI:10.1093/advances/nmab049).
[35] Srour, B., Kordahi, M. C., Bonazzi, E., Deschasaux-Tanguy, M., Touvier, M. & Chassaing, B. 2022 Ultra-processed foods and human health: from epidemiological evidence to mechanistic insights. *Lancet Gastroenterol Hepatol* **7**, 1128-1140. (DOI:10.1016/s2468-1253(22)00169-8).
[36] Dicken, S. J. & Batterham, R. L. 2021 The Role of Diet Quality in Mediating the Association between Ultra-Processed Food Intake, Obesity and Health-Related Outcomes: A Review of Prospective Cohort Studies. *Nutrients* **14**. (DOI:10.3390/nu14010023).
[37] Tobias, D. K. & Hall, K. D. 2021 Eliminate or reformulate ultra-processed foods? Biological mechanisms matter. *Cell Metab* **33**, 2314-2315. (DOI:10.1016/j.cmet.2021.10.005).
[38] Hall, K. D., Farooqi, I. S., Friedman, J. M., Klein, S., Loos, R. J. F., Mangelsdorf, D. J., O'Rahilly, S., Ravussin, E., Redman, L. M., Ryan, D. H., et al. 2022 The energy balance model of obesity: beyond calories in, calories out. *Am J Clin Nutr* **115**, 1243-1254. (DOI:10.1093/ajcn/nqac031).
[39] Hall, K. D. 2018 Did the Food Environment Cause the Obesity Epidemic? *Obesity (Silver Spring)* **26**, 11-13. (DOI:10.1002/oby.22073).
[40] Hall, K. D., Ayuketah, A., Brychta, R., Cai, H., Cassimatis, T., Chen, K. Y., Chung, S. T., Costa, E., Courville, A., Darcey, V., et al. 2019 Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake. *Cell Metab* **30**, 67-77.e63. (DOI:10.1016/j.cmet.2019.05.008).
[41] Rolls, B. J. 2009 The relationship between dietary energy density and energy intake. *Physiol Behav* **97**, 609-615. (DOI:10.1016/j.physbeh.2009.03.011).
[42] Fazzino, T. L., Courville, A. B., Guo, J. & Hall, K. D. 2023 Ad libitum meal energy intake is positively influenced by energy density, eating rate and hyper-palatable food across four dietary patterns. *Nature Food* **4**, 144-147. (DOI:10.1038/s43016-022-00688-4).
[43] de Graaf, C. & Kok, F. J. 2010 Slow food, fast food and the control of food intake. *Nature reviews. Endocrinology* **6**, 290-293. (DOI:10.1038/nrendo.2010.41).
[44] Forde, C. G., Mars, M. & de Graaf, K. 2020 Ultra-Processing or Oral Processing? A Role for Energy Density and Eating Rate in Moderating Energy Intake from Processed Foods. *Current developments in nutrition* **4**, nzaa019. (DOI:10.1093/cdn/nzaa019).
[45] Teo, P. S., Lim, A. J., Goh, A. T., R, J., Choy, J. Y. M., McCrickerd, K. & Forde, C. G. 2022 Texture-based differences in eating rate influence energy intake for minimally processed and ultra-processed meals. *Am J Clin Nutr* **116**, 244-254. (DOI:10.1093/ajcn/nqac068).
[46] Fazzino, T. L., Rohde, K. & Sullivan, D. K. 2019 Hyper-Palatable Foods: Development of a Quantitative Definition and Application to the US Food System Database. *Obesity (Silver Spring)* **27**, 1761-1768. (DOI:10.1002/oby.22639).
[47] DiFeliceantonio, A. G., Coppin, G., Rigoux, L., Edwin Thanarajah, S., Dagher, A., Tittgemeyer, M. & Small, D. M. 2018 Supra-Additive Effects of Combining Fat and Carbohydrate on Food Reward. *Cell Metab* **28**, 33-44.e33. (DOI:10.1016/j.cmet.2018.05.018).
[48] de Araujo, I. E., Schatzker, M. & Small, D. M. 2020 Rethinking Food Reward. *Annu Rev Psychol* **71**, 139-164. (DOI:10.1146/annurev-psych-122216-011643).
[49] Small, D. M. & DiFeliceantonio, A. G. 2019 Processed foods and food reward. *Science* **363**, 346-347. (DOI:10.1126/science.aav0556).
[50] Gearhardt, A. N. & DiFeliceantonio, A. G. 2022 Highly processed foods can be considered addictive substances based on established scientific criteria. *Addiction*. (DOI:10.1111/add.16065).
[51] Kelly, A. L., Baugh, M. E., Oster, M. E. & DiFeliceantonio, A. G. 2022 The impact of caloric availability on eating behavior and ultra-processed food reward. *Appetite* **178**, 106274. (DOI:10.1016/j.appet.2022.106274).

[52] Wyatt, P., Berry, S. E., Finlayson, G., O'Driscoll, R., Hadjigeorgiou, G., Drew, D. A., Khatib, H. A., Nguyen, L. H., Linenberg, I., Chan, A. T., et al. 2021 Postprandial glycaemic dips predict appetite and energy intake in healthy individuals. *Nat Metab* **3**, 523-529. (DOI:10.1038/s42255-021-00383-x).
[53] Hall, K. D. 2019 Challenges Interpreting Inpatient and Outpatient Human Nutrition Studies. *Cell Metab* **30**, 227-228. (DOI:10.1016/j.cmet.2019.06.015).
[54] Martinez Steele, E., Raubenheimer, D., Simpson, S. J., Baraldi, L. G. & Monteiro, C. A. 2018 Ultra-processed foods, protein leverage and energy intake in the USA. *Public Health Nutr* **21**, 114-124. (DOI:10.1017/s1368980017001574).
[55] Raubenheimer, D. & Simpson, S. J. 2019 Protein Leverage: Theoretical Foundations and Ten Points of Clarification. *Obesity (Silver Spring)* **27**, 1225-1238. (DOI:10.1002/oby.22531).
[56] Simpson, S. J. & Raubenheimer, D. 2005 Obesity: the protein leverage hypothesis. *Obes Rev* **6**, 133-142. (DOI:10.1111/j.1467-789X.2005.00178.x).
[57] Hall, K. D. 2019 The Potential Role of Protein Leverage in the US Obesity Epidemic. *Obesity (Silver Spring)* **27**, 1222-1224. (DOI:10.1002/oby.22520).
[58] Gimeno, R. E., Briere, D. A. & Seeley, R. J. 2020 Leveraging the Gut to Treat Metabolic Disease. *Cell Metab* **31**, 679-698. (DOI:10.1016/j.cmet.2020.02.014).
[59] Aguilera, J. M. 2019 The food matrix: implications in processing, nutrition and health. *Critical reviews in food science and nutrition* **59**, 3612-3629. (DOI:10.1080/10408398.2018.1502743).
[60] Heindel, J. J., Howard, S., Agay-Shay, K., Arrebola, J. P., Audouze, K., Babin, P. J., Barouki, R., Bansal, A., Blanc, E., Cave, M. C., et al. 2022 Obesity II: Establishing causal links between chemical exposures and obesity. *Biochem Pharmacol* **199**, 115015. (DOI:10.1016/j.bcp.2022.115015).
[61] Lefferts, L. 2023 Obesogens: Assessing the Evidence Linking Chemicals in Food to Obesity. (Washington D.C., The Center for Science in the Public Interest.
[62] Schatzker, M. 2021 *The end of craving: Recovering the lost wisdom of eating well*. New York, Avid Reader Press; 257 p.
[63] Alvheim, A. R., Malde, M. K., Osei-Hyiaman, D., Lin, Y. H., Pawlosky, R. J., Madsen, L., Kristiansen, K., Frøyland, L. & Hibbeln, J. R. 2012 Dietary linoleic acid elevates endogenous 2-AG and anandamide and induces obesity. *Obesity (Silver Spring)* **20**, 1984-1994. (DOI:10.1038/oby.2012.38).
[64] Simopoulos, A. P. 2016 An Increase in the Omega-6/Omega-3 Fatty Acid Ratio Increases the Risk for Obesity. *Nutrients* **8**, 128. (DOI:10.3390/nu8030128).
[65] Watkins, B. A. & Kim, J. 2014 The endocannabinoid system: directing eating behavior and macronutrient metabolism. *Frontiers in psychology* **5**, 1506. (DOI:10.3389/fpsyg.2014.01506).
[66] Hall, K. D., Guo, J., Dore, M. & Chow, C. C. 2009 The progressive increase of food waste in America and its environmental impact. *PLoS One* **4**, e7940.