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News and Views

The "Novelty-as-Scarcity" Hypothesis: An Evolutionary Hypothesis to Partially Explain the Global Obesity Epidemic

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Abstract

The "novelty-as-scarcity" hypothesis proposes that the consumption of novel foods or foods with non-traditional food component ratios, or novel processing methods, are interpreted by the body as fallback foods and produce a false signal of imminent food scarcity, thereby triggering (chronic) fat accumulation. This framework is rooted in the evolutionary principle that the ability to store fat was crucial for survival during periods of unpredictable food availability. Today, this may pose an "evolutionary mismatch". The paper lists plausible biological mechanisms, from the initial sensing of novel food components to their metabolic effects, that could lead to increased fat accumulation. Observations supporting this hypothesis include weight gain among migrants adopting new dietary habits and rising fattening rates in developing countries with exposure to Westernized foods. The novelty-as-scarcity hypothesis implies that standardized dietary recommendations might be suboptimal if they disregard an individual's historical dietary background.

Keywords: obesity; evolutionary mechanisms; evolutionary mismatch; fallback foods; novel foods

1. Introduction

In the foreword to a book titled "Obesity in America" published in 1979, George A. Bray [1] pointed out the "epidemic proportion of obesity" in the US and its association with negative health consequences. Since then, the obesity epidemic has spread worldwide, with an estimated increase in the global obesity prevalence by 155.1% in males and 104.9% in females between 1990 and 2021 [2]. The most widely believed explanation for these uninterrupted and continuing trends is the overconsumption of calories, that in turn is believed to be caused by the increasing global availability of cheap, processed and calorically dense foods. However, as argued by Mozaffarian [3], this explanation is not only oversimplified but also inconsistent with data showing rising obesity rates despite a plateau or decline of energy intake and availability and a modest increase in physical activity in the US after the year 2000. This author therefore proposed to look for complex biological interactions between the human body, its microbiome and the food environment, including putative population changes in the gut microbiome, metabolic expenditure, and intergenerational transmission of risk.

Lifestyle factors play a major role in the prevention and treatment of obesity and related diseases such as type II diabetes. Accordingly, the field of lifestyle medicine, which involves diet, exercise, sleep, stress, and other lifestyle modifications, appears very promising for preventing and treating obesity [4]. The Mediterranean diet in particular has been shown to improve body composition and metabolic health to a greater degree than other officially recommended diets [5,6]. This diet, or better yet dietary pattern, is based on whole foods traditionally consumed in the Mediterranean region including, but not limited to, fruits, vegetables, sourdough bread, fish and olive oil, resulting in lower carbohydrate and higher protein and fat content than most officially recommended diets [7]. Another dietary pattern with a similar macronutrient profile is the so-called Paleolithic diet, which excludes evolutionarily novel foods such as grains and legumes and has also been shown to reduce body mass index (BMI) and body fat more than other recommended diets (although sample sizes were generally small in these studies) [8,9,10].

In this article, we argue that both the Mediterranean and the Paleolithic diet are effective in obesity prevention and treatment, because they rely on whole foods with a long history of human consumption. More generally, we extend the list of possible drivers of the global obesity epidemic by proposing a new evolutionary hypothesis that is centered on ancient mechanisms to sense the novelty of foods and link them to environmental conditions.

The capacity to anticipate future environmental conditions, particularly the availability of essential resources like food, would have conferred a substantial survival benefit to organisms. Animals that could interpret subtle environmental cues to predict periods of scarcity prior to the actual appearance of food shortage could proactively adjust their behavior and physiology; for instance, by increasing their body fat reserves before the shortage fully manifested.

According to the "dual intervention point" (DIP) model of body fat regulation, evolutionary pressures selected for mechanisms to avoid both critically low and high levels of body fat because on the one hand fat serves as a buffer against both starvation and illness, such as anorexia; and on the other hand too much body fat increases predation risk [11]. Evolutionary biologists have also proposed the "insurance hypothesis", which states that animals and humans increase their body fat mass during times of ecological instability as an insurance against anticipated future food scarcity [12,13].

Here, we propose a new hypothesis that introduces a nuanced dimension to this:

The consumption of novel foods, or unfamiliar ratios of food components such as macronutrients—a hallmark of non-traditional diets—is perceived by the body as 'fallback food'. This signals imminent food scarcity and triggers evolutionarily preserved mechanisms of fat accumulation.

We call this the "novelty-as-scarcity" (NAS) hypothesis. We believe that this hypothesis partly explains the current obesity epidemic by attributing it to global dietary transitions that expose a large part of the world population to novel foods and food components.

This paper is organized as follows. In section 2, we briefly review how the body is able to sense and perceive food novelty, which is the prerequisite for our hypothesis. Next, in section 3 we assemble and discuss several potential signals caused by food novelty that could trigger a consequent fat accumulation process, thus supporting the NAS hypothesis. Section 4 extends on these data by summarizing evidence from observational studies that the discussed mechanisms play a role in human fat mass gain. Finally, section 5 discusses the NAS hypothesis and its limitations regarding scientific testing and summarizes the main conclusions.

2. Sensory Detection of Dietary Novelty: The Initial Interface With the Environment

2.1 Olfactory and Gustatory Systems: Identifying the Unfamiliar

The primary interface between an animal and its potential food sources is mediated by the olfactory (smell) and gustatory (taste) systems. These chemosensory systems enable the organism to identify food, assess its quality, and distinguish between familiar and unfamiliar items. Odor and taste receptors, upon encountering novel chemical signatures not previously experienced, can trigger a range of initial behavioral responses, from neophobia (the avoidance of novelty) to neophilia (an exploratory engagement with novelty) [14].

The olfactory system plays a particularly crucial role in this process. The olfactory system has direct and rapid neuroanatomical connections to key hypothalamic regions, such as the arcuate nucleus, which houses critical neuronal cell populations involved in the central regulation of energy balance [15]. This suggests a direct pathway through which information about food novelty, perceived via olfaction, can swiftly influence metabolic control centers. The gustatory system, consisting of taste receptors in the oral cavity as well as in the gastrointestinal tract, works in concert with olfaction to contribute to the overall flavor perception, and also has direct links to brain regions such as the hypothalamus and limbic system, which control emotional and metabolic responses to food [16].

Beyond the detection of novel compounds, the absence of familiar, reassuring olfactory and gustatory cues associated with known, safe, and nutritious foods could constitute a significant signal. If a potential food item lacks the characteristic sensory profile of a reliable nutrient source (e.g., the scent of ripe fruit or the savory notes of cooked meat), the brain might interpret this not merely as "novel" but as "potentially suboptimal" or "indicative of a degraded food environment". This involves more than just identifying a new molecule; it is about the overall sensory gestalt failing to match an established "safe and nutritious" template. Furthermore, these sensory systems are capable of learning and forming associations between specific food ingestion cues and their post-ingestive consequences [17]. An initially novel food, if consistently proven to be calorically valuable and non-toxic, might see its "novelty" signal diminish in importance. Conversely, if novel foods are frequently associated with low nutritional yield or mild malaise, the novelty cue itself could become a stronger predictor of poor foraging outcomes, reinforcing a scarcity-like metabolic response. This explains why artificial non-caloric sweeteners have been shown to induce weight gain in many rodent studies independent from caloric intake and are associated with weight gain in large-scale cohort studies in a dose-dependent manner (reviewed in [18]). Sucralose, for example, induces hepatic fat accumulation in mice independent from caloric intake by activating taste receptor type 1 member 3 in hepatocytes [19]. In a clinical study investigating the effects of daily supplementation with sucrose, sucralose or steviol glycosides over six weeks, only the sucralose group gained weight despite a concurrent significant reduction in caloric intake [20].

2.2 Food Neophobia: Behavioral and Potential Metabolic Implications of Avoiding Novelty

Food neophobia, characterized by a reluctance to consume unfamiliar foods, is a widespread behavioral trait observed in many omnivorous species, including humans. It is generally considered an adaptive evolutionary mechanism designed to protect individuals from ingesting potentially harmful or toxic substances [21]. This innate caution towards the unknown highlights a pre-existing biological sensitivity to food novelty.

Research has linked high levels of food neophobia with several dietary and health-related outcomes. Individuals exhibiting strong food neophobia often have reduced dietary variety and lower overall quality and are more likely

to develop adverse metabolic profiles and obesity [22,23]. These findings suggest a potential, albeit possibly indirect, connection between an organism's behavioral response to novel foods and its underlying metabolic regulation.

Within the framework of our hypothesis, the degree of an individual's innate neophobia could determine the strength of the "novelty-as-scarcity" signal. A stronger physiological "scarcity" signal in individuals with high food neophobia could be due to heightened perceived risk, or an amplified stress response associated with consuming something aversive, thereby potentiating fat storage to a greater extent than in a neophilic individual who consumes the same novel food out of curiosity. The context of novel food consumption is therefore critical: consumption driven by necessity in the face of dwindling familiar options (as the hypothesis implies) is distinct from exploratory tasting or gradual habituation, where the "novelty-as-scarcity" signal might be attenuated or absent.

3. Candidate Biological Mechanisms Linking Fallback/Novel Food Intake to Fat Accumulation

We here review several candidate mechanisms or "proximate causes" whose interplay could translate a "fallback/novel food" signal into a physiological drive for increased fat accumulation. These mechanisms include neuroendocrine signaling, immune responses, and cellular nutrient sensing.

3.1 Neuroendocrine Signaling Cascades: Translating Fallback/Novelty Into Metabolic Shifts

Neuroendocrine pathways are central to regulating energy homeostasis and could be key in mediating the proposed response to dietary fallback/novelty.

3.1.1 The Gut-Brain Axis: Altered Satiety and Nutrient Sensing With Unfamiliar Foods

The gut-brain axis represents a critical bidirectional communication system where ingested nutrients trigger signals from the gastrointestinal tract to the central nervous system (CNS), profoundly influencing food intake, energy expenditure, and nutrient partitioning. Enteroendocrine cells lining the gut possess sophisticated chemosensory machinery, including G-protein coupled receptors and solute transporters, which detect preabsorptive nutrients [24]. Upon nutrient or bitter compound detection, these cells release a variety of gut peptides, such as cholecystokinin (CCK) in the duodenum, glucagon-like peptide-1 (GLP-1) in the ileum, and the di-peptide tyrosine-tyrosine (PYY) in the colon (as a result of short-chain fatty acid detection) [16]. These hormones can act locally on vagal afferent nerves or enter circulation to act directly on the CNS, particularly the brainstem and hypothalamus, to orchestrate appropriate metabolic responses, including the induction of satiety and modulation of energy expenditure [24].

Novel or historically unrecognized food components might interact differently with these gut-based nutrient sensors compared to familiar foods. They could bind with lower affinity, activate different receptor subtypes, or fail to activate certain pathways altogether. Furthermore, the gut microbiota, which plays a significant role in digesting complex food components and influencing gut hormone release [24], may not be adapted to efficiently process these novel substrates. This could lead to an altered profile or magnitude of gut hormone release. For instance, a calorically equivalent load of novel food might elicit a weaker or delayed release of satiety hormones like GLP-1 or PYY compared to a familiar meal. This is supported by an acute randomized feeding study, in which a Paleolithic diet meal elicited significantly higher plasma concentrations of GLP-1 and PYY than an energy- and macronutrient-matched control diet that included more evolutionarily novel foods such as rice [25]. An attenuated satiety signal upon ingestion of novel foods could be interpreted by the brain as indicative of lower-than-expected nutrient yield or quality. This misinterpretation mimics a state of relative nutrient scarcity, thereby promoting compensatory behaviors like increased food seeking or, as hypothesized, a metabolic shift towards increased fat storage to buffer against this perceived unreliability of the food source. The brain relies on these gut signals not only for caloric accounting but also for information about macronutrient composition [16,24]. Novel food components could disrupt this precise signaling, leading to "nutrient confusion" and a default to a conservative, energy-storing strategy.

The gut microbiota's role is particularly pertinent here. A novel food might introduce substrates for which the existing microbial community is ill-equipped, leading to inefficient fermentation, the production of an unusual profile of metabolites (e.g., different types or ratios of short-chain fatty acids), or even dysbiosis [26]. These microbial shifts can, in turn, alter gut peptide secretion and directly influence host metabolism, potentially generating signals that the brain interprets as nutrient stress or scarcity, thereby favoring fat accumulation [27].

3.1.2 Hypothalamic Integration: Modulating Energy Balance in Response to Perceived Environmental Instability

The hypothalamus fine-tunes appetite, energy expenditure, and ultimately, body weight. Signals indicating food novelty, potentially relayed from the sensory systems or via the gut-brain axis, could be interpreted by hypothalamic circuits as evidence of environmental instability or a decline in the quality and reliability of available food sources.

This interpretation could lead to an upward adjustment in the "set point" of the defended level of adiposity [11], effectively programming the body to favor fat accumulation as a buffer against anticipated future hardships. Key hypothalamic neuropeptides, including leptin, insulin, neuropeptide Y (NPY), Agouti-related peptide (AgRP), and

pro-opiomelanocortin (POMC), are central to this regulation [28]. Their expression levels can be modulated through phytochemicals and micronutrients [29], providing a putative link between both the presence of novel and the absence of familiar food components and hypothalamic energy balance regulation. For example, leptin, a hormone secreted by adipose tissue in proportion to fat mass, normally acts on the hypothalamus to reduce food intake and increase energy expenditure [30]. However, under a perceived threat signaled by dietary novelty, the sensitivity to leptin might decrease (leptin resistance), or the drive to store fat might functionally override leptin's typical anorexigenic effects. This is supported by a study showing that digested wheat gluten, an evolutionarily novel food component for humans, inhibits binding between leptin and its receptor [31]. The brain might prioritize the perceived future threat of scarcity over the current reality of adequate or even increasing fat stores. This represents a shift from simple reactive homeostasis, which corrects current energy deficits, to a form of predictive allostasis, where the body proactively alters its internal state to meet anticipated future demands by defending a higher level of body fat [32].

3.1.3 Stress-Related Pathways: Potential Activation of the HPA Axis by Dietary Uncertainty

The consumption of unfamiliar foods, particularly if this experience is coupled with neophobia-related anxiety or is interpreted as a sign of a deteriorating or uncertain food environment, has the potential to activate the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of glucocorticoids like cortisol [33].

Chronic or repeated activation of this stress pathway can have significant metabolic consequences. Elevated cortisol levels are known to promote visceral fat accumulation, increase appetite (particularly for energy-dense, palatable foods), and alter overall metabolic programming. If the introduction of novel foods into the diet is perceived as a stressor, this could initiate a hormonal cascade favoring fat deposition. There is evidence that individuals with hyperresponsiveness of the HPA axis are particularly predisposed to obesity [34]. This could be translated to individuals with high food neophobia who are compelled to eat novel foods due to a lack of familiar alternatives. Beyond psychological stress, novel food components that are poorly metabolized or place an unusual burden on the body's detoxification pathways could induce a form of "metabolic stress" at the cellular level. This, in turn, might trigger systemic stress responses or feed into inflammatory pathways, further contributing to a metabolic state conducive to fat storage.

3.2 Immune System Engagement: Metabolic Inflammation as a Response to Novel Dietary Components

The immune system is increasingly recognized as a critical player in metabolic regulation. In metabolic tissues such as adipose tissue, the liver, and even the hypothalamus, certain dietary components can trigger immune cell activation, leading to a state of chronic, low-grade inflammation often termed "metabolic inflammation" or "meta-inflammation" [35]. This sub-clinical inflammation is a hallmark of fattening and is implicated in the development of insulin resistance and other metabolic dysfunctions.

Novel or historically unrecognized food ingredients, such as those found in many ultra-processed foods (e.g., certain synthetic emulsifiers, artificial sweeteners, novel lipid structures, or preservatives), can not only lead to immune dysregulation through their impact on the microbiome, but also by inducing chronic oxidative stress and low-grade inflammation [36]. This immune dysregulation can result in the production and release of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6. Locally and systemically, most pro-inflammatory cytokines promote the development of insulin resistance [37], which can fuel a vicious cycle in which insulin resistance increases blood glucose levels and promotes the ectopic accumulation of lipids in organs like the liver and skeletal muscle.

The concept of "trained immunity" further suggests that innate immune cells can develop a form of immunological memory through long-term epigenetic reprogramming after contact with pathogens. Following an initial inflammatory challenge, such as exposure to a high-sugar diet or potentially a novel food component, these cells can exhibit an enhanced or altered response upon a secondary challenge [38]. This could mean that continued exposure to a diet rich in novel components might lead to progressively exacerbated inflammatory responses, perpetuating metabolic dysfunction and fat accumulation. In ancient environments such internal inflammatory states might have correlated with periods of injury, infection, or environmental insecurity; these are conditions often co-occurring with food scarcity.

3.3 Novel Macronutrient Ratios and Their Effect on Cellular Signaling Pathways

At the cellular level, intricate nutrient-sensing pathways continuously monitor the internal milieu, gauging energy status (e.g., ATP/AMP ratio) and the availability of key metabolites such as glucose, amino acids, and fatty acids. Key players in these pathways include AMP-activated protein kinase (AMPK) and the mechanistic target of rapamycin (mTOR), which are affected by hormones such as insulin, insulin-like growth factor-1 (IGF-1) and growth hormone [39].

Through their activation in various organs, in particular the hypothalamus and white adipose tissue, these nutrient sensing pathways may exert a net fat-storing effect when stimulated by diets with a macronutrient composition that is novel from an evolutionary standpoint [40]. For example, the natural species-specific diet of rodents is high in carbohydrates and low in fat, and laboratory rodents fed chow with 70% energy from carbohydrates and 10% from fat do not get obese [41]. A prediction of our hypothesis

is that rodents should gain fat mass when fed diets with novel macronutrient compositions compared to their ancestral diet. Indeed, many mouse strains become obese when fed diets with higher fat and lower carbohydrate content, with peak effects observed at 20% carbohydrate and 60% fat content (by energy) [42]. Hu et al. [42] have shown that there were significantly positive associations between the dietary fat levels and hypothalamic insulin signaling, IGF-1 signaling and the growth hormone receptor as well as with the modulation of hypothalamic mTOR signaling. In white adipose tissue, 46/152 genes in the mTOR signaling pathway correlated significantly to dietary fat content, while there was no significant change in the expression of mTOR itself.

In contrast to mice, a variety of evidence supports the assumption that humans have evolved on highly carnivorous hunter-gatherer diets and are therefore accustomed to lower carbohydrate and higher fat and protein intake [43,44]. In a large survey of followers of a modern carnivore diet, the average BMI decreased from a pre-diet value of 27.2 [23.5–31.9] kg/m^2 to 24.3 [22.1–27.0] kg/m^2 (p = 0.01, n = 1229), and even greater reductions were reported by individuals with type I and II diabetes [45]. However, the NAS hypothesis also allows for the possibility that, depending on local ecology and geography, populations may have become adapted to higher carbohydrate diets in the sense that the consumed carbohydrate-rich foods lost their novelty after being frequently consumed for many generations. This appears to be the case for recent hunter-gatherers such as the Hadza or horticulturalists such as the Tsimane whose diets are richer in carbohydrates than typical Western diets [46]. In particular, Pontzer et al. [46] pointed out that wild honey, which consists primarily of glucose and fructose, constitutes a significant source of calories for many hunter-gatherers, yet apparently does not induce fat mass gain. This is explained by the NAS hypothesis if we consider both the sensory gestalt and nutrient matrix of wild honey to be an ancient and familiar food for humans. At the same time, the NAS hypothesis predicts that modern high-carbohydrate diets would promote fat mass gain in humans that have not historically adapted to such high levels of carbohydrates or the sources of these carbohydrates that come from novel foods.

Besides the macronutrient ratios per se, it is also conceivable that any novel relative proportion of macronutrient subtypes will be interpreted by the body as forthcoming shortage and trigger fat accumulation. Such are for example fatty acids of various chain length and saturation or the proportion of glucose, fructose and starch among dietary carbohydrates.

For example, while the muscle of wild ruminants, which were humans' main source of fatty acids, contain on average 43% saturated, 35% monounsaturated and 22% polyunsaturated fatty acids (PUFA) (see Table 7 in Ref. [47]) modern diets usually include a higher proportion of PUFA, since in the second half of the 20th century seed oils became a major component of the Western diet and largely replaced animal fats [48]. The omega-6 PUFA linoleic acid which composes most of seed oils, is obesogenic when eaten in excess to omega-3 PUFAs [49]. Likewise, a high proportion of fructose in the diet, which nowadays is easily achieved by the abundance of high-fructose corn syrup in foods, is obesogenic in rats [50] and causes liver fattening and insulin resistance in humans [51].

4. Initial Observations in Support of the Hypothesis

Extant hunter-gatherer populations can serve as models to test explanations and predictions of evolutionary mismatch hypotheses such as our NAS hypothesis [46]. In particular, despite important differences in the ecological environment of recent and Paleolithic hunter gatherers, the diet of African hunter-gatherers has been extensively used to infer general characteristics of Paleolithic human diets [52]. While the global prevalence of obesity (BMI >30 kg/m^2) in 2021 was estimated as 20.8% (95% Bayesian uncertainty interval 20.5–21.1%) in females and 14.8% (14.6–15.0%) in males, respectively [2], it is generally less than 1% in extant hunter-gatherers [46]. Although the hunter-gatherer lifestyle certainly differs in more respects from most modern-day lifestyles than just diet, the relative lack of evolutionary novel foods in hunter-gatherer diets might at least partly explain this difference in obesity rates.

Accordingly, two meta-analyses of randomized controlled trials, which partly included individuals with obesity and type II diabetes, revealed that modern versions of a Paleolithic diet result in significantly larger reductions of BMI, body weight and fat mass compared to officially recommended diets [8,9]. These meta-analyses support our hypothesis, because the Paleolithic diet by definition excludes evolutionarily novel foods such as grains, milk products, legumes and industrially processed foods, while officially recommended diets frequently advise the consumption of less animal foods and more whole grain products. Another study on breast cancer patients undergoing radiotherapy also showed significant reductions in BMI and body fat mass by a Paleolithic lifestyle intervention consisting of a Paleolithic diet and daily outdoor activity compared to a propensity-score matched control group on a standard diet, showing how diet can be integrated with other lifestyle modifications to achieve benefits [53].

Further evidence for the NAS hypothesis comes from dietary transition studies. A systematic review of dietary transitions in four populations for which detailed data on lifestyle factors were available indicates that dietary novelty is more strongly associated with rising obesity rates than increased calories, reduced physical activity or other factors [54]. A particularly noteworthy transition among three of these populations (Yemenite Jews, Tokelauans and Maasai) was the transition to lower total and saturated fat and a compensatory higher intake of refined carbohydrates.

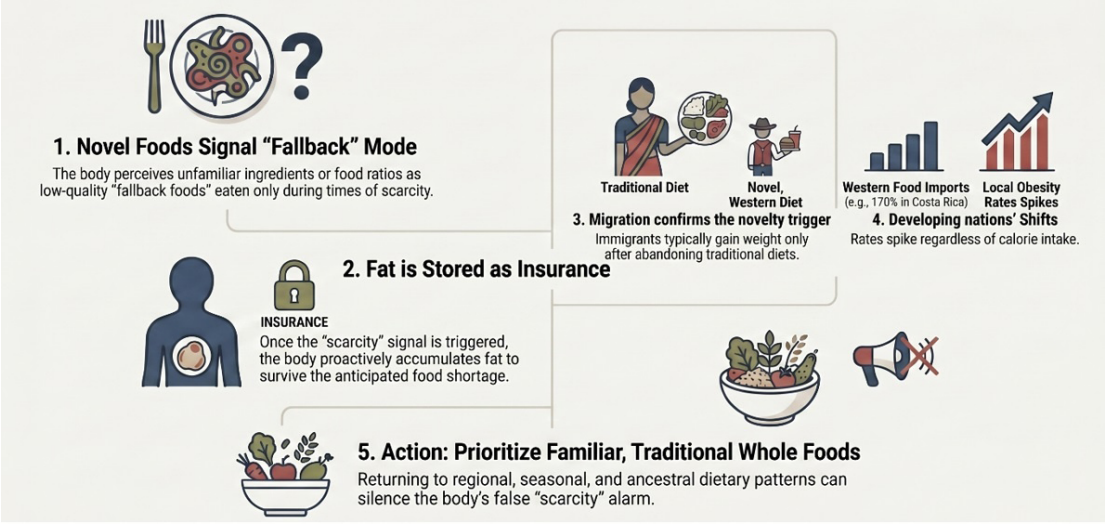

Fig. 1. Mechanisms and implications of the novelty-as-scarcity hypothesis. More details are described in the text.

This transition had a strong association with increased obesity and type II diabetes rates [54], consistent with the predictions of the NAS hypothesis.

Another example are the Tsimane horticulturalists from Bolivia that traditionally consume a high-carbohydrate, high-fiber and low-fat diet and have very low obesity rates, indicating that they are well adapted to their agricultural foods, i.e., these foods are no longer novel to them. Using dietary recall data spanning a period of 5.5 years, Kraft et al. [55] were able to document a dietary transition in the Tsimane population towards a significant increase in the consumption of sugar and seed oils. This transition resulted in an overall increase in calorie and carbohydrate consumption and was accompanied by an increase in BMI, body fat percentage and obesity rates.

Developing countries like China and India are also experiencing rising rates of obesity concurrent with the introduction of novel Western foods [56]. Another example is Costa Rica, where tourism is a major part of the economy and food imports rose by 170% between 1992 and 2005, with concurrently rising obesity rates [57]. In these examples, it is unlikely that chronic stress is the main factor driving the increasing obesity rates. Further evidence that novel foods are one of the main factors comes from studies on migrating populations that undergo nutrition transitions in foreign countries. Here, the overall picture is consistent with obesity developing to a larger degree the more immigrants give up their traditional dietary habits. For example, while adoption of a typical Western diet is associated with obesity, there are also examples where migrants exhibit better health than non-migrants if they retain some of their traditional dietary habits [57].

The above cited studies on populations experiencing increasing rates of obesity after dietary transitions would not constitute evidence for the NAS hypothesis if other, more simple explanations exist for these observations. We argue that this is not the case. For example, the argument that an increase in caloric consumption accompanying a dietary transition from a traditional to a novel diet causes fat mass gains is rejected by the fact that hunter-gatherer diets have energy densities that overlap with those of industrialized populations [46]. Likewise, total energy expenditure of small-scale societies can be quite similar compared to industrialized populations when adjusted for differences in fat-free mass [46], contradicting the hypothesis that a decrease in energy expenditure is responsible for fat mass gains after migration of populations into a new geographical region. Also, as pointed out by Mozaffarian [3], calorie consumption in the US more or less stagnated and physical activity levels slightly increased, while obesity rates continued to rise. Thus, the fact that novel foods replaced more traditional foods due to changing industrial production or the migration of certain populations, appears to be one plausible explanation for the lasting obesity epidemic in light of the mechanisms outlined in the previous sections.

5. Limitations of Our Hypothesis

In its current formulation, the NAS hypothesis is of a very broad scope, which limits its experimental confirmation or falsification, respectively. Testing of the hypothesis faces various methodological challenges such as defining and standardizing "novelty", individual response variability, distinguishing between long- and short-term effects, confounding factors, and the relative effect of the presence and absence of food components; most of these challenges are generally common in dietary research. A crucial question to be answered by future studies is what defines the "reference diet" or "reference food" relative to which another diet or food should be considered novel for a given organism. A gradual transition of foods between fallback/novel to normal foods is expected in traditional stable societies such that foods that are considered normal will be

perceived by the body of non-members as fallback/novel. Populations of the so-called "Blue Zones" [58] or the Tsimane [46] that consume traditionally treated agricultural foods are examples that indicate that populations can adapt to relatively novel, post-Paleolithic foods as 'regular'. The time range for such an adaptation is unknown however. In the case of humans, the study of ancestral diets and traditional dietary variation across the globe will be helpful to solve this problem. As shown in Section 4, using data from dietary transitions could also be helpful; however, a differentiation of the NAS hypothesis from hypotheses that attribute obesity to transitions towards higher caloric density or less physical activity can be difficult, because these hypotheses are not mutually exclusive. Finally, we admit that some aspects of our hypothesis are currently speculative and lack direct evidential support, such as that individuals with a higher degree of food neophobia are more susceptible to the fat-storing signal induced by novel foods. Nevertheless, this assumption is principally open to experimental confirmation or falsification, which should be undertaken by future studies.

6. Summary and Conclusions

The ability to store fat in anticipation of food scarcity, once useful, may present challenges in contemporary food environments. The proportion of macronutrients, fatty acid chain length and degree of saturation, amino acid patterns, phytochemicals and other food components in contemporary diets differ from past traditional diets and, in many cases, diets to which humans during the Paleolithic era would have had access. If these deviations from ancestral diets indeed act as a biological signal for potential future food shortages and trigger an adaptive mechanism to accumulate more fat, this would present an evolutionarily grounded framework for understanding one potential contributor to modern metabolic disease (Fig. 1). The plausibility of our hypothesis is supported by the existence of multiple interconnected biological systems capable of detecting and responding to dietary novelty, although future experimental verification is needed for the hypothesis that these novelty signals indeed translate into fat mass gain.

The overall response may also depend on a "novelty threshold": a minor dietary change might elicit little response, whereas a diet substantially composed of evolutionarily novel ingredients, such as many ultra-processed foods, could surpass this threshold and trigger more significant metabolic adaptations.

Due to this complexity, as we have pointed out, testing of the NAS hypothesis faces various methodological challenges. However, future research may be aimed at identifying specific foods with high detrimental potential, identifying specific novelty biomarkers including alterations of microbiomes, and effects of novel foods during critical developmental stages.

The practical implication of this hypothesis is that the common obesogenic or anti-obesogenic perception of different foods, like green salads or fats, is not absolute but relative to an individual historical base and hence, that following global or state level standardized recommendations could be detrimental to the health of an individual person. We propose that public health would benefit more from evolutionarily informed and individualized lifestyle medicine approaches, involving dietary advice that emphasizes regional, seasonal and traditionally prepared foods.

Ultimately, this line of inquiry underscores a fundamental theme in metabolic physiology: mechanisms that were once vital for survival in ancestral environments characterized by food unpredictability can become maladaptive when confronted with the unprecedented dietary landscape of the modern world.

Author Contributions

Conceptualization: MBD; investigation: MBD, RJK; writing—Original draft preparation: MBD, RJK. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

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The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used Google Gemini (version 1.5 Pro; Google LLC, Mountain View, CA, USA) in order to list potential biological mechanisms and check English wording. Fig. 1 was produced with the help of Google NotebookLM (version powered by Gemini 3 Pro; Google LLC, Mountain View, CA, USA). The authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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