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The "Novelty-as-Scarcity" Hypothesis: An Evolutionary Explanation for the Global Obesity Epidemic

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Abstract: The "Novelty-as-Scarcity" (NAS) hypothesis proposes that the consumption of novel foods or foods with non-traditional food component ratios or processing methods is interpreted by the body as 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". Although defining and isolating "novelty" poses methodological challenges, the NAS hypothesis has 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 obesity rates in developing countries with exposure to Westernized foods. The NAS hypothesis implies that standardized dietary recommendations might be suboptimal if they disregard an individual's historical dietary background.

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I. Introduction: The Evolutionary Imperative for Fat Regulation and the "Novelty-as-Scarcity-Indicator" Hypothesis

We hypothesize that the consumption of novel foods or unfamiliar ratios of food components such as macronutrients, a common feature of the Western diet, are perceived by the body as imminent food scarcity and trigger chronic fat accumulation.

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 hand fat serves as a buffer against both starvation and illness anorexia and on the other hand too much body increases predation risk (Speakman & Elmquist, 2022). Evolutionary biologists have 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 (Bateson & Pepper, 2023; Haig, 2023). The current hypothesis introduces a nuanced dimension to this, suggesting that qualitative changes to the species-specific or familiar diet could be interpreted by the body as a harbinger of resource decline, prompting a preemptive increase in energy reserves. The appearance of novel foods might not simply signal that "a new food is available," but rather that "familiar, reliable food sources are becoming scarce." This interpretation implies that dietary novelty

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acts as a proxy for declining stability or quality of established food resources. This is what we call the "Novelty-as-scarcity" (NAS) hypothesis.

Studies have shown that food insecurity can lead to weight gain, proposed as an adaptive "insurance" policy against an uncertain future (Bateson & Pepper, 2023; Wilbrecht et al., 2024). NAS extends this by proposing that the novelty is a specific type of cue the body interprets as indicative of environmental deterioration and potential future food insecurity. This interpretation is nuanced: signal might not be an absolute absence of calories but rather a decline in the availability of *optimal* or *familiar* caloric sources. The body, despite receiving adequate calories from these new sources, might still perceive negative environmental changes and initiate fat accumulation as a precautionary measure.

We used Gemini LLM to create a list of potential food novelty signaling and consequent fat accumulation processes. We meticulously reviewed the list and eliminated not sufficiently supported processes, adding our chosen citations in items we considered to have a hypothesis validation potential.

II. Sensory Detection of Dietary Novelty: The Initial Interface with the Environment

A. 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 (Hadley et al., 2004). 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) (Puleo et al., 2021).

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 (Guzmán-Ruiz et al., 2021). 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, contributes to the overall flavor perception and also has direct links to brain regions, like the hypothalamus and limbic system, that control emotional and metabolic responses to food (San Gabriel, 2015).

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's 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 cues and their post-ingestive consequences (Stark et al., 2024). 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.

B. 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

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harmful or toxic substances (Santisi et al., 2021). 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 may consume a diet of lower overall quality (Knaapila et al., 2015; Sarin et al., 2019). Food neophobia may also be associated with adverse metabolic profiles, including obesity, decreased omega-3 fatty acid concentrations, increased fasting serum insulin levels and a higher risk of developing type 2 diabetes (Knaapila et al., 2015; Proserpio et al., 2018; Sarin et al., 2019). 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.

III. Candidate Biological Mechanisms Linking Novel Food Intake to Fat Accumulation

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

A. Neuroendocrine Signaling Cascades: Translating Novelty into Metabolic Shifts

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

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 (Bauer et al., 2016). Enteroendocrine cells lining the gut possess sophisticated chemosensory machinery, including G-protein coupled receptors (GPCRs) and solute transporters, which detect preabsorptive nutrients (Bauer et al., 2016). 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) (San Gabriel, 2015). 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 (Bauer et al., 2016).

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 (Bauer et al., 2016), 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

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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 (Bligh et al., 2015). An attenuated or "confusing" 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 might mimic 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 (Bauer et al., 2016; San Gabriel, 2015); novel 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 (Feng et al. 2025, Rondinella et al.2025). 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 (Amabebe et al., 2020).

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" or the defended level of adiposity (Speakman & Elmquist, 2022), 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 (Arora, 2006; Coll et al., 2007). Their expression levels can be modulated through phytochemicals and micronutrients (Aragones et al., 2016) providing a putative link between the presence of novel or 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 (Myers et al., 2008). 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 (Cordain, 1999), inhibits binding between leptin and its receptor (Jönsson et al., 2015). 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 (McEwen & Wingfield, 2003).

3. Stress-Related Pathways: Potential Activation 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 body’s physiological stress response systems. These include the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of glucocorticoids like cortisol, and the sympathetic nervous system, which releases catecholamines (Goldstein, 2003).

Chronic or repeated activation of these stress pathways can have significant metabolic consequences. Elevated cortisol levels, for instance, are known to promote the accumulation of

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visceral fat, 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 (Rodriguez et al., 2015). 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.

B. 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" (Ramos-Lopez et al., 2022; Shapiro et al., 2011). This sub-clinical inflammation is a hallmark of obesity 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 UPFs (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 (Leo et al., 2021). This immune dysregulation can result in the production and release of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-1β. These cytokines can then act locally and systemically to impair insulin signaling, alter adipocyte function (promoting lipid storage and inhibiting lipolysis), and contribute to the ectopic accumulation of lipids in organs like the liver and muscle (Lyons et al., 2016).

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 (Ochando et al., 2022). 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. Evolutionary, such internal inflammatory states might have correlated with periods of injury, infection, or environmental insecurity, conditions often co-occurring with food scarcity.

C. 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 (Yuan et al., 2013). 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. These sensors and their downstream effectors coordinate cellular metabolic responses, shifting between anabolism (building and storing) and catabolism (breaking down for energy) based on nutrient availability and cellular needs.

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 (Cofnas, 2016). 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

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(Hall et al., 2022). A prediction of our hypothesis is that rodents should gain fat mass when fed diets with novel macronutrient composition 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) (Hu et al., 2018). Hu et al. 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 (Hu et al. 2018).

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 (Ben-Dor et al., 2021; Klement, 2022). Hence, our hypothesis predicts that modern high-carbohydrate diets would promote fat mass gain in humans that have not historically adapted to high levels of carbohydrates. This is consistent with the carbohydrate-insulin model, according to which carbohydrates via their impact on insulin release, promote substrate partitioning towards fat deposition (Astley et al., 2018; Ludwig, 2023; Soto-Mota et al., 2023). Insulin spikes result in cellular uptake of nutrients with subsequent activation of the mTOR pathway, but subsequent dips in blood glucose in the postprandial period have been shown to be associated with increased appetite, which could drive higher energy intake and fat mass gain (Wyatt et al., 2021).

Besides the macrunutrient 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 fats of various chain length and saturation or the proportion of glucose, fructose and starch among dietary carbohydrates.

For example, while the muscle of wild ruminates which were humans' main source of fats contain on average 43% saturated, 35% monounsaturated and 22% polyunsaturated fats (PUFA)(Cordain et al., 2002:Table 7) modern diets usually include a higher proportion of PUFA as of the second half of the 20th century seed oils became a major components of the Western diet largely replacing animal fats and other traditional sources of dietary fat (Simopoulos, 2016). The omega-6 PUFA linoleic acid which composes most of seed oils, is obesogenic when eaten in excess to omega-3 PUFAs (Jeong et al., 2024). 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 (Bocarsly et al., 2010) and probably humans, too (Bray et al., 2004).

IV. Initial Observations in Support of the Hypothesis

Migrating from a homeland to a foreign country as a transition from one food culture to another is bound to associate migrants with novel foods. Authors attribute weight gain among migrants to dietary acculturation (Delavari et al., 2013), acculturative stress (Tseng & Fang, 2011), and lower physical activity (Jakicic et al., 2019; Kinra et al., 2020).

Developing countries like China and India are experiencing rising rates of obesity concurrent with the introduction of novel Western foods (Astrup et al., 2008; Bhattacharya, 2014).Since there is less stress associated with this phenomenon we can assume that its contribution to migrants' weight gain is minimal.

These observation can be contrasted with the relative health, including low rates of obesity, among populations of the so-called "Blue Zones" (Buettner & Skemp, 2016) that consume traditionally treated agricultural foods (David, 2024), indicating that populations can adapt to regard relatively novel, post-Paleolithic foods as 'regular'. However, this observation may also imply that novelty can be in the processing, or rather the lack of it, of food prior to its consumption.

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V. 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 that humans during the Paleolithic era would have had access to (Ben-Dor et al., 2021; Goedeke et al., 2024). 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 evolutionary grounded framework for understanding one potential contributor to modern metabolic disease. The plausibility of our hypothesis is supported by the existence of multiple interconnected biological systems capable of detecting and responding to dietary novelty.

The initial detection of dietary novelty occurs via the sensory systems, particularly olfaction and gustation, which identify unfamiliar chemical signatures and relay this information to the central nervous system, including key regulatory areas like the hypothalamus.

Simultaneously, the gut-brain axis processes the ingested novel components. Differences in how these components interact with gut nutrient sensors or are metabolized by the gut microbiota could lead to altered satiety and nutrient signaling profiles (e.g., modified release of GLP-1, PYY) compared to familiar foods, potentially mimicking signals of undernutrition or poor food quality. The immune system, particularly within metabolic tissues, may recognize certain novel food ingredients as foreign or as danger signals, initiating a low-grade inflammatory response ("meta-inflammation") characterized by the release of pro-inflammatory cytokines that can directly impair insulin signaling and promote lipid storage (Lyons et al., 2016).

At the cellular level, nutrient-sensing pathways (e.g. mTOR) may be stimulated by unfamiliar macronutrient components of novel diets in ways that shift cellular priorities towards energy conservation. These diverse peripheral and cellular signals converge on central neuroendocrine pathways, particularly within the hypothalamus. Here, they are integrated with other inputs to modulate appetite, energy expenditure, and potentially activate stress hormone cascades (e.g., HPA axis, leading to cortisol release), which can further favor fat accumulation.

These mechanisms form a complex network with considerable cross-talk and feedback loops. For instance, inflammation triggered by the immune system can alter hypothalamic sensitivity to metabolic hormones like leptin and insulin (Lyons et al., 2016). 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 UPFs (Cotter et al., 2021), could surpass this threshold and trigger significant metabolic adaptations.

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 which are common to most dietary research.

Future research may be aimed at identifying specific foods with high detrimental potential, identifying specific novelty biomarkers including alterations of microbiomes, and effect 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, following global or state level standardized recommendations could be detrimental to health.

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.

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References

1. Amabebe, E., Robert, F. O., Agbalalah, T., & Orubu, E. S. (2020). Microbial dysbiosis-induced obesity: role of gut microbiota in homoeostasis of energy metabolism. *British Journal of Nutrition*, *123*(10), 1127–1137.
2. Aragones, G., Ardid-Ruiz, A., Ibars, M., Suarez, M., & Bladé, C. (2016). Modulation of leptin resistance by food compounds. *Molecular Nutrition & Food Research*, *60*(8), 1789–1803.
3. Arora, S. (2006). Role of neuropeptides in appetite regulation and obesity–a review. *Neuropeptides*, *40*(6), 375–401.
4. Astley, C., Todd, J., Salem, R., Vedantam, S., Ebbeling, C., Huang, P., Ludwig, D., Hirschhorn, J., & Florez, J. (2018). Genetic Evidence That Carbohydrate-Stimulated Insulin Secretion Leads to Obesity. *Clinical Chemistry*, *64 1*, 192–200. https://doi.org/10.1373/clinchem.2017.280727
5. Astrup, A., Dyerberg, J., Selleck, M., & Stender, S. (2008). Nutrition transition and its relationship to the development of obesity and related chronic diseases. *Obesity Reviews*, *9*. https://doi.org/10.1111/j.1467-789X.2007.00438.x
6. Bateson, M., & Pepper, G. V. (2023). Food insecurity as a cause of adiposity: evolutionary and mechanistic hypotheses. *Philosophical Transactions of the Royal Society B*, *378*(1888), 20220228.
7. Bauer, P. V., Hamr, S. C., & Duca, F. A. (2016). Regulation of energy balance by a gut–brain axis and involvement of the gut microbiota. *Cellular and molecular life sciences*, *73*, 737–755.
8. Ben-Dor, M., Sirtoli, R., & Barkai, R. (2021). The evolution of the human trophic level during the Pleistocene. *American Journal of Physical Anthropology*, *175*(S72), 27–56. https://doi.org/https://doi.org/10.1002/ajpa.24247
9. Bhattacharya, C. (2014). Fast food and obesity in India. *International Journal of Marketing and Technology*, *4*, 100–109.
10. Bligh, H. F. J., Godsland, I. F., Frost, G., Hunter, K. J., Murray, P., MacAulay, K., Hyliands, D., Talbot, D. C., Casey, J., & Mulder, T. P. (2015). Plant-rich mixed meals based on Palaeolithic diet principles have a dramatic impact on incretin, peptide YY and satiety response, but show little effect on glucose and insulin homeostasis: an acute-effects randomised study. *British journal of nutrition*, *113*(4), 574–584.
11. Bocarsly, M. E., Powell, E. S., Avena, N. M., & Hoebel, B. G. (2010). High-fructose corn syrup causes characteristics of obesity in rats: increased body weight, body fat and triglyceride levels. *Pharmacology Biochemistry and Behavior*, *97*(1), 101–106.
12. Bray, G. A., Nielsen, S. J., & Popkin, B. M. (2004). Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *The American Journal of Clinical Nutrition*, *79*(4), 537–543.
13. Buettner, D., & Skemp, S. (2016). Blue Zones. *American Journal of Lifestyle Medicine*, *10*, 318–321. https://doi.org/10.1177/1559827616637066
14. Cofnas, N. (2016). Methodological problems with the test of the Paleo diet by Lamont et al. (2016). *Nutrition & Diabetes*, *6*. https://doi.org/10.1038/nutd.2016.22
15. Coll, A. P., Farooqi, I. S., & O'Rahilly, S. (2007). The hormonal control of food intake. *Cell*, *129*(2), 251–262.
16. Cordain, L. (1999). Cereal grains: humanity's double-edged sword. *World Review of Nutrition and Dietetics*, *84*, 19–19.
17. Cordain, L., Watkins, B. A., Florant, G., Kelher, M., Rogers, L., & Li, Y. (2002). Fatty acid analysis of wild ruminant tissues: evolutionary implications for reducing diet-related chronic disease. *European Journal of Clinical Nutrition*, *56*(3), 181–191.
18. Cotter, T., Kotov, A., Wang, S., & Murukutla, N. (2021). 'Warning: ultra-processed'—A call for warnings on foods that aren't really foods. *BMJ Global Health*, *6*(12), e007240.

 doi:10.20944/preprints202506.0419.v1

19. David, T. (2024). A Comprehensive Review of Traditional Food Processing Methods and Their Effects on Food Security. *International Journal of Agricultural and Life Sciences*. https://doi.org/10.22573/spg.ijals.024.s122000121
20. Delavari, M., Sønderlund, A. L., Swinburn, B., Mellor, D., & Renzaho, A. (2013). Acculturation and obesity among migrant populations in high income countries–a systematic review. *BMC Public Health*, *13*, 1–11.
21. Goedeke, S., Murphy, T., Rush, A., & Zinn, C. (2024). Assessing the Nutrient Composition of a Carnivore Diet: A Case Study Model. *Nutrients*, *17*(1), 140.
22. Goldstein, D. S. (2003). Catecholamines and stress. *Endocrine Regulations*, *37*(2), 69–80.
23. Guzmán-Ruiz, M. A., Jiménez, A., Cárdenas-Rivera, A., Guerrero-Vargas, N. N., Organista-Juárez, D., & Guevara-Guzmán, R. (2021). Regulation of metabolic health by an "olfactory-hypothalamic axis" and its possible implications for the development of therapeutic approaches for obesity and T2D. *Cellular and Molecular Neurobiology*, 1–17.
24. Hadley, K., Orlandi, R. R., & Fong, K. J. (2004). Basic anatomy and physiology of olfaction and taste. *Otolaryngologic Clinics of North America*, *37*(6), 1115–1126.
25. Haig, D. (2023). Fat as insurance, leanness as bodily display: did Ronald Reagan make us fat? *Journal of Bioeconomics*, *25*(3), 225–238.
26. Hall, K., Farooqi, I., Friedman, J., Klein, S., Loos, R., Mangelsdorf, D., O'Rahilly, S., Ravussin, E., Redman, L., Ryan, D., Speakman, J., & Tobias, D. (2022). The energy balance model of obesity: beyond calories in, calories out. *The American Journal of Clinical Nutrition*. https://doi.org/10.1093/ajcn/nqac031
27. Hu, S., Wang, L., Yang, D., Li, L., Togo, J., Wu, Y., Liu, Q., Li, B., Li, M., Wang, G., Zhang, X., Niu, C., Li, J., Xu, Y., Couper, E., Whittington-Davies, A., Mazidi, M., Luo, L., Wang, S.,…Speakman, J. (2018). Dietary Fat, but Not Protein or Carbohydrate, Regulates Energy Intake and Causes Adiposity in Mice. *Cell Metabolism*, *28 3*, 415–431. https://doi.org/10.1016/j.cmet.2018.06.010
28. Jakicic, J. M., Powell, K. E., Campbell, W. W., Dipietro, L., Pate, R. R., Pescatello, L. S., Collins, K. A., Bloodgood, B., Piercy, K. L., & Committee, P. A. G. A. (2019). Physical activity and the prevention of weight gain in adults: a systematic review. *Medicine and Science in Sports and Exercise*, *51*(6), 1262.
29. Jeong, H. Y., Moon, Y. S., & Cho, K. K. (2024). ω-6 and ω-3 polyunsaturated fatty acids: Inflammation, obesity and foods of animal resources. *Food Science of Animal Resources*, *44*(5), 988.
30. Jönsson, T., Memon, A. A., Sundquist, K., Sundquist, J., Olsson, S., Nalla, A., Bauer, M., & Linse, S. (2015). Digested wheat gluten inhibits binding between leptin and its receptor. *BMC biochemistry*, *16*, 1–5.
31. Kinra, S., Mallinson, P. A. C., Cresswell, J. A., Bowen, L. J., Lyngdoh, T., Prabhakaran, D., Reddy, K. S., Vaz, M., Kurpad, A. V., & Davey Smith, G. (2020). Relative contribution of diet and physical activity to increased adiposity among rural to urban migrants in India: A cross-sectional study. *PLoS Medicine*, *17*(8), e1003234.
32. Klement, R. J. (2022). Was there a need for high carbohydrate content in Neanderthal diets? *American Journal of Biological Anthropology*, *179*(4), 668–677.
33. Knaapila, A. J., Sandell, M. A., Vaarno, J., Hoppu, U., Puolimatka, T., Kaljonen, A., & Lagström, H. (2015). Food neophobia associates with lower dietary quality and higher BMI in Finnish adults. *Public Health Nutrition*, *18*(12), 2161–2171.
34. Leo, E. E. M., Peñafiel, A. M., Escalante, V. M. H., & Araujo, Z. M. C. (2021). Ultra-processed diet, systemic oxidative stress, and breach of immunologic tolerance. *Nutrition*, *91*, 111419.
35. Ludwig, D. (2023). Carbohydrate-insulin model: does the conventional view of obesity reverse cause and effect? *Philosophical Transactions of the Royal Society B: Biological Sciences*, *378*. https://doi.org/10.1098/rstb.2022.0211

 doi:10.20944/preprints202506.0419.v1

36. Lyons, C. L., Kennedy, E. B., & Roche, H. M. (2016). Metabolic inflammation-differential modulation by dietary constituents. *Nutrients*, *8*(5), 247.
37. McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. *Hormones and behavior*, *43*(1), 2–15.
38. Myers, M. G., Cowley, M. A., & Münzberg, H. (2008). Mechanisms of leptin action and leptin resistance. *Annual Review of Physiology*, *70*(1), 537–556.
39. Ochando, J., Mulder, W., Madsen, J., Netea, M., & Duivenvoorden, R. (2022). Trained immunity — basic concepts and contributions to immunopathology. *Nature Reviews. Nephrology*, *19*, 23–37. https://doi.org/10.1038/s41581-022-00633-5
40. Proserpio, C., Laureati, M., Invitti, C., & Pagliarini, E. (2018). Reduced taste responsiveness and increased food neophobia characterize obese adults. *Food Quality and Preference*, *63*, 73–79.
41. Puleo, S., Braghieri, A., Pacelli, C., Bendini, A., Toschi, T. G., Torri, L., Piochi, M., & Di Monaco, R. (2021). Food Neophobia, odor and taste sensitivity, and overall flavor perception in food. *Foods*, *10*(12), 3122.
42. Ramos-Lopez, O., Martinez-Urbistondo, D., Vargas-Nuñez, J. A., & Martinez, J. A. (2022). The role of nutrition on meta-inflammation: insights and potential targets in communicable and chronic disease management. *Current Obesity Reports*, *11*(4), 305–335.
43. Rodriguez, A. C. I., Epel, E. S., White, M. L., Standen, E. C., Seckl, J. R., & Tomiyama, A. J. (2015). Hypothalamic-pituitary-adrenal axis dysregulation and cortisol activity in obesity: a systematic review. *Psychoneuroendocrinology*, *62*, 301–318.
44. San Gabriel, A. M. (2015). Taste receptors in the gastrointestinal system. *Flavour*, *4*(1), 14.
45. Santisi, G., Magnano, P., & Scuderi, V. E. (2021). Food Neophobia and food disgust: The mediating role of perceived vulnerability to disease. *Behavioral Sciences*, *11*(5), 65.
46. Sarin, H. V., Taba, N., Fischer, K., Esko, T., Kanerva, N., Moilanen, L., Saltevo, J., Joensuu, A., Borodulin, K., & Männistö, S. (2019). Food neophobia associates with poorer dietary quality, metabolic risk factors, and increased disease outcome risk in population-based cohorts in a metabolomics study. *The American Journal of Clinical Nutrition*, *110*(1), 233–245.
47. Shapiro, H., Lutaty, A., & Ariel, A. (2011). Macrophages, meta-inflammation, and immuno-metabolism. *The scientific world journal*, *11*(1), 2509–2529.
48. Simopoulos, A. P. (2016). An increase in the omega-6/omega-3 fatty acid ratio increases the risk for obesity. *Nutrients*, *8*(3), 128.
49. Soto-Mota, A., Pereira, M., Ebbeling, C., Aronica, L., & Ludwig, D. (2023). Evidence for the carbohydrate-insulin model in a reanalysis of the Diet Intervention Examining The Factors Interacting with Treatment Success (DIETFITS) trial. *The American Journal of Clinical Nutrition*. https://doi.org/10.1016/j.ajcnut.2022.12.014
50. Speakman, J. R., & Elmquist, J. K. (2022). Obesity: an evolutionary context. *Life metabolism*, *1*(1), 10–24.
51. Stark, R., Dempsey, H., Kleeman, E., Sassi, M., Osborne-Lawrence, S., Sheybani-Deloui, S., Rushby, H. J., Mirth, C. K., Austin-Muttitt, K., & Mullins, J. (2024). Hunger signalling in the olfactory bulb primes exploration, food-seeking and peripheral metabolism. *Molecular Metabolism*, *89*, 102025.
52. Tseng, M., & Fang, C. Y. (2011). Stress is associated with unfavorable patterns of dietary intake among female Chinese immigrants. *Annals of Behavioral Medicine*, *41*(3), 324–332.
53. Wilbrecht, L., Lin, W. C., Callahan, K., Bateson, M., Myers, K., & Ross, R. (2024). Experimental biology can inform our understanding of food insecurity. *Journal of Experimental Biology*, *227*(Suppl_1), jeb246215.
54. Wyatt, P., Berry, S., Finlayson, G., O'Driscoll, R., Hadjigeorgiou, G., Drew, D., Khatib, H., Nguyen, L., Linenberg, I., Chan, A., Spector, T., Franks, P., Wolf, J., Blundell, J., & Valdes, A. (2021). Postprandial

 doi:10.20944/preprints202506.0419.v1

glycaemic dips predict appetite and energy intake in healthy individuals. *Nature metabolism*, *3*, 523–529. https://doi.org/10.1038/s42255-021-00383-x

55. Yuan, H.-X., Xiong, Y., & Guan, K.-L. (2013). Nutrient sensing, metabolism, and cell growth control. *Molecular cell*, *49*(3), 379–387.