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Food in an Evolutionary Context: Insights from Mother's Milk

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Abstract

In the emergence of diverse animal life forms, food is the most insistent and pervasive of environmental pressures. As the life sciences begin to understand organisms in genomic detail, evolutionary perspectives provide compelling insights into the results of these dynamic interactions between food and consumer. Such an evolutionary perspective is particularly needed today in the face of unprecedented capabilities to alter the food supply. What should we change? Answering this question for food production, safety, and sustainability will require a much more detailed understanding of the complex interplay between humans and their food. Many organisms that we grow, produce, process, and consume as foods naturally evolved adaptations in part to avoid being eaten. Crop breeding and processing have been the tools to convert overtly toxic and anti-nutritious commodities into foods that are safe to eat. Now the challenge is to enhance the nutritional quality and thereby contribute to improving human health. We posit that the Rosetta stone of food and nourishment is mammalian lactation and "mother's milk." The milk that a mammalian mother produces for her young is a complete and comprehensive diet. Moreover the capacity of the mammary gland as a remarkable bioreactor to synthesize milk, and the infant to utilize milk, reflects 200 million years of symbiotic co-evolution between producer and consumer. Here we present emerging trans-disciplinary research "decoding" mother's milk from humans and other mammals. We further discuss how insights from mother's milk have important implications for food science and human health.

Keywords

lactation; infant development; gene-culture co-evolution; dairy; personalized medicine; obesity; nutrition; mammalian evolution

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Introduction

The world is facing a major challenge: advances in agriculture in the 20th century dramatically improved productivity enabling enough food for 7 billion people. However, this chemistry-dominated, petroleum-driven industry is proving not only to be unsustainable energetically, but equally disturbingly is not providing optimally healthy foods. Diet dependent chronic diseases are continuing to increase and are now the leading causes of death throughout the world. Agriculture and food will need to be reconsidered. A key question is what constitutes healthy food? How can diet promote health, prevent diseases, protect individuals and enhance their performance? To answer these questions, we will need to embrace the integrative nature of biology, increasing diversity, sustainability and health. Evolutionary biology provides a unique scientific perspective to illuminate our understanding of food. Firstly, in order for something to be food, something else must be consuming it. And since both of these “things” are biological, they are themselves the products of the evolutionary process of natural selection through which adaptations are generated. Secondly, foods and their consumers often co-evolve in mutually beneficial ways, i.e. they are part of their respective selective environments. A well-cited example of plant-animal mutualism is the seed dispersal actions of mammals and birds. The animals, as consumers, gain nutrients and calories from the fruit matrix containing the seeds. These seeds often pass undigested through the intestinal tract to then be distributed kilometers away. In this way seeds do not compete with their parent for light, water or soil nutrients by attempting to germinate in their parent's shade.[1]

By studying the diverse interactions between plant and animal species from the perspective of this evolutionary dynamic, it has been possible to broaden our understanding of the complexity of food itself. Biological systems are a continuously recycling process, and in the larger sense we are all ‘food’ to something at some point. However, the immediacy of the selective pressure on various organisms as food varies widely. Furthermore, the capabilities of modern agriculture; genetics and directed breeding, food processing and product formulation has positioned humans to achieve unprecedented control of their personal health through diet.

The most elegant and compelling example of the symbiotic co-evolution between producer and consumer is the milk synthesized by a mammalian mother for her infant. For our purposes here, “milk” represents the conceptual construct of all mammalian milks, except where illustrative examples from specific taxa are indicated. Of additional note, here we distinguish human milk from breast-feeding, a more complex and diverse spectrum of behavioral and physiological processes than simply the transfer of milk.[2] Mother's milk provides a unique model for investigating food and nutrition because milk reflects both the outcome and the processes of natural selection. The adaptive properties in milk are generated by selection acting upon variation among individuals within species. Indeed lactation strategies vary among species[3,4] and milk synthesis varies among individuals within species.[4] Thus, milk can be considered the result of a biological process shaped by selective pressure to process maternal diets and tissues into a complete nutrition resource for offspring. Discouragingly, the myriad health, nutritional, and protective consequences of this mammary bioprocess remain poorly understood. Additionally, early infancy is the one point in the life cycle in which mammalian young are consuming a single food source. This is in stark contrast to the varied diets mammals consume post-weaning, particularly humans. Hence milk is a profoundly informative model for complete nourishment and the targets, mechanisms, and benefits that a protective diet can provide.

At its core, milk is a nutrient delivery system. Though simple in concept, transferring all essential nutrients in appropriate amounts from maternal diet and body stores via milk to a mammalian infant are daunting. The bioavailability of most nutrients from food materials is poor due to their insolubility, reactivity, or complexation. Furthermore, nutrients as consumed are absorbed to varying extents that are in turn contingent to some extent on the presence and concentration of other nutrients in the diet. Understanding these relationships have been developed largely by painstaking research on the absorption of nutrients from complex food matrices, for example, the absorption of dietary iron is now known to be enhanced by vitamin C and inhibited by phytates.[5] Understanding more complex issues of nutrition in the same molecular detail, by identifying and controlling for the complexities of dietary intake in adults, becomes quickly insurmountable in part because dietary intake varies so widely among individuals. Mother's milk makes such investigations much more tractable by virtue of milk being the sole food consumed during early infancy in all mammals.

Milk as a model of overall nourishment can illuminate other dimensions of diet and health. For example, nutritional conditions during early development shape, or rather *program*, physiology and neurobiology with life-long consequences for metabolism, health, cognition, and behavior.[6] This further complicates investigations of food and nutrition in adults; utilization of food does not just reflect the complexity of the diverse adult diet as stated above, but is also contingent on physiological pathways established during development unique to their early environment. Understanding the dynamics of early food consumption, e.g. mother's milk, is therefore emerging as a vital dimension of early nourishment and particularly for optimizing health in later life.

Mother's Milk: Evolutionary Perspectives

The traditional view of milk is of a simple liquid with essential nutrients. Such a view ignores the dimensions of milk as personal, dynamic, active, and structured. The milk of each mammalian species is measurably, and not surprisingly, unique. The presence and concentration of constituents in mammalian milks, reflect their evolutionary history, their current ecology, and the developmental trajectories of their young. For example, in arctic marine environments, lipids are necessary for the massive fuel demands of thermogenesis. Hooded seal pups (*Cystophora cristata*) are born on unstable ice floes in the North Atlantic, and their dams lactate for only four days before weaning them. Consequently the fat concentration in hooded seal milk is the highest known among mammals (>60%) and dams transfer 7kg of lipids via milk to the pups each day of lactation. These accelerated lipid transfer rates are similarly dependent on ‘herculean’ lipolysis rates to release the complex triglycerides for absorption within the intestine of the seal pups. The benefits of this spectacular energy transfer is that the pups can establish a dense fat layer to sustain them after weaning before they are proficient at catching fish.7 In contrast, among primates, including humans, infants grow relatively slowly over a long period. The period of lactational investment of these primates is thus prolonged. Primate milk is relatively dilute, with low fat and protein concentrations and high water content.

These fascinating variations in macronutrient composition among species have to some extent disguised the deeper complexity of milk. Beyond the macro-constituents that provide calories to the infant, e.g. fat, protein, and sugar, mother's milk contains immunoglobulins, minerals, vitamins, hormones, bacteria, and oligosaccharides.[4] A small, but growing body of literature is revealing the breadth of nutritional functions of these components. For example, research has shown that specific micro-constituents of milk, alone and in concert, contribute to neurobiological, cognitive, somatic, metabolic, and immune development in infants.[4,8-9]

Importantly not only does milk composition vary among species, milk composition varies among mothers within species.[4] In this way infants receive “personalized” milk from their mother. For example, among humans and non-human primates, milk fatty acids are derived from the immediate diet, maternal tissue stores, and mammary biosynthesis. Hence the lipid composition reflects maternal dietary intakes both during lactation and in the months and even years prior to lactation.[10] Extensive research effort has been dedicated to long-chain polyunsaturated fatty acids (LCPUFA), specifically the omega-3 fatty acids; docosahexaenoic acid (DHA) and its precurser alpha-linolenic acid (ALA). Research has demonstrated that fatty acid concentrations vary among human mothers.[11] LCPUFA supply developmental assembly processes of neurological tissues that are critical for neurodevelopment and cognition, though mechanistic details remain maddeningly vague.[9] In addition to acute dietary intake, LCPUFA are mobilized from maternal somatic lipid stores.[9] As a result, infants are buffered from their mother's short-term dietary fluctuations in fatty acid consumption.

Moreover, naturally occurring individual differences in milk synthesis have the potential to calibrate or program individual developmental trajectories. Among rhesus monkeys, individual differences in milk energy density (kcal/g), yield, and cortisol concentrations, have been implicated in infant growth rate and behavioral development.[12-14] Rhesus macaques (*Macaca mulatta*) are a particularly valuable animal model for investigating properties of milk that influence infant developmental trajectories. The divergence between the macaque and human lineage occurred ~25 MYA, they are the most common non-human primate biomedical model, and their genome has been sequenced.[15] Moreover, rhesus and humans usually produce singleton infants that grow and develop in the context of a complex social network.[13] For these reasons, results from rhesus are compellingly translatable to mechanisms of similar higher order functions in humans.

Few dimensions of milk and lactation reflect the principle of evolution as splendidly as the relationship between milk and the establishment and maintenance of the infant's microbiota.[16] For example, milk includes highly selective oligosaccharides that support the growth of only a very unique group of intestinal bacteria (*Bifidobacteria longum biovar infantis*) that co-evolved with mammals.[17] Milk thus amplifies its biological impact by guiding the development and phenotype of a bacterial ecosystem that serves to assist the infant with additional digestive, metabolic, and immunological functions. Research has now demonstrated that humans are adapted to produce a substantial number of complex free oligosaccharides, secreted into milk on average an order of magnitude more than do our non-human primate relatives.[4] These oligosaccharides are not digested by the infant, nor are they digestible by simple bacteria. Rather they are the primary food source for the narrow group of beneficial commensal gut bacteria that possess the genetic capability to breakdown the complex milk oligosaccharides, particularly *Bifidobacterium longum infantis*.[16] *Bifidobacteria infantis* are critical for health and nutrition because they modulate immune responses in the intestine and participate in the bioconversion of digested nutrients.[18] Moreover *Bifidobacteria infantis* serve as competitive inhibitors of the establishment of more pathogenic bacteria implicated in chronic infant diarrhea, a leading cause of childhood mortality worldwide.[19]

The co-evolution of the human genes that code for the production of milk oligosaccharides and the bacteria that digest them illuminates how natural selection produces complex adaptations. At its most elemental, this remarkable system of nourishment has emerged from intensive selective pressure in which mothers simultaneously synthesize food for their infant and food for the intestinal bacteria that optimize that infant's assimilation of his food. As a result, mothers aren't just eating for two, they are actually eating for $2*10^{11}$ (their own intestinal microbiome, as well as their infant's)!

Mother's milk does not only provide the nutritional substrate for the establishment of commensal bacteria, milk continues to inoculate the neonate with bacteria. In rhesus macaques, mother's milk includes numerous beneficial lactic acid bacteria that are translocated from the mother's gut, via an as yet unknown pathway, to the mammary gland to be vertically transmitted to the infant post-natally.[20] Lactic acid bacteria contribute to digestive lipolysis and proteolysis and the assimilation of calcium, phosphorus, and iron, and produce metabolites that inhibit the establishment of pathogenic microbes.[18-19] Bacteria of maternal intestinal origin have also been identified in the milk of humans and rodents, but much remains to be understood about the mechanism of translocation and function of these bacteria when ingested by the developing young.[19-20]

Discouragingly, the diversity of milk's components and their functions remain poorly researched and largely under-appreciated. Although documented on occasion, most research on the health consequences of milk constituents derives from comparisons between commercial formula and breast-milk and solely in terms of essential nutrient status. Future research should systematically investigate the many sources and diverse consequences of inter-individual differences in milk composition among breast-feeding mothers. For example, individual human and macaque mothers vary in the diversity and prevalence of oligosaccharides and bacteria in their milk, however the source of that variation, and the consequences for individual infants, has not yet been explained. Understanding the specific ways in which milk is “personalized”- the magnitude and sources of inter-individual variation in milk constituents, and the consequences for the infant- will be instrumental for improving commercial formulas and providing translatable insights into adult nutrition.

Others' Milk: Gene-Culture Co-Evolution

Humans are particularly rare among animals in that we no longer rely exclusively on natural selection to optimize the food we eat, rather we have been conspicuously successful at artificially selecting the attributes we want to optimize in the plants and animals we consume. A prime example of this is the cultural practices of dairying that emerged subsequent to the domestication of the cattle, sheep, and goats 5,000-10,000 years ago.[21] This advance in our agricultural technology, domesticating animals and the consumption of “others' milk,” however, resulted in natural selection favoring genetic mutations in some populations of humans that practiced animal husbandry, a phenomena known as gene-culture co-evolution.[22] Mammalian infants, reliant on mother's milk, produce lactase only until weaning, after which the ability to digest lactose is lost in all other examined mammals. A subset of humans, however, have evolved the ability to digest lactose into adulthood, an adaptation so favored by natural selection that the frequency of these allelic mutations are present in some form among the majority of humans living today.[22] Specifically, singular and compound allelic mutations underlie the lactase persistence that allows many humans to digest the lactose in dairy products.[23] Our understanding of milk, both human and cow, is thusly enhanced by an evolutionary perspective.

The gene-culture co-evolution demonstrated by the example of dairying described above, illustrates the broader principle of how culture changed the human genome. Culture may have to change, however, in response to advances in genomic sciences. In China, researchers are inserting human DNA into transgenic cloned dairy cows. This genomic manipulation has produced cows that express human-type lactoferrin and lysozyme in cow's milk.[24-25] Lactoferrin and lysozyme are immune constituents with anti-bacterial properties that are found in higher concentrations in human breast milk than in cow's milk. This species difference suggests that these constituents are relatively more important for the immunological function and development of the human neonate. This technology has the potential to benefit human health and improve infant formula, however many consumers are resistant, or even hostile, to inserting human DNA into dairy species.[26] We know, however, that humans share significant portions of our genomic structure with the chimpanzee, the mouse, and even the sea cucumber. In other words, a considerable fraction of genes in the human genome are already in animal genomes, and vice versa, by virtue of evolution. Together advances in dairying practices combined with greater scientific literacy have the potential to change culture perceptions of genetically modified milk in the coming decade.

Implications for Human Health

Although culture has the potential to change quite quickly, natural selection shapes the genome over a longer timescale.[27] For example, the physiological and neurobiological mechanisms of eating, tasting, digesting, and metabolizing our food[28] were quite adaptive under ancestral environmental conditions. In our evolutionary past, earlier *Homo* species hunted and gathered across wide distances and relied substantially on a variety of plant materials available seasonally.[29] The vast majority of individuals were likely at neutral energy balance in that the daily energy they expended in behavioral activity closely matched the energy they consumed. Ancestrally when individuals encountered rare foods rich in sugars, fats, and salt, the dopaminergic "reward" circuitry in the brain was activated. This triggered feelings of pleasure and precipitated gorging, a very useful tactic if the future availability of high value foods was uncertain in a variable landscape.[30]

Our dietary ecology in the modern world, however, is characterized by ubiquitous "fast foods"- highly digestible and energetically dense- and once adaptive genes for metabolic efficiency are increasingly maladaptive as they contribute to excessive weight gain and even more destructively, a variety of metabolic dysfunctions.[30] Importantly, only a few generations, in a subset of human populations, have experienced this nutritional environment of commercial food and especially conspicuous caloric abundance. Consequently, insufficient time has passed for random recombinations and mutations to arise that produce metabolic pathways that are less efficient or able to adapt the fuel supply to productive activity. Instead we carry around "evolutionary baggage" in the form of genes that contribute to the over-consumption of fuels that, when combined with a sedentary lifestyle, are efficiently stored on our bodies rather than directed successfully to enhanced health and performance.

We are not, however, the hostage of our genome. Phenotype is the product of genes *and environment*. Although our genes reflect an ancestral past so divergent from the modern world, modifying the early dietary environment is an important opportunity to shape a healthy phenotype. For example, the neural circuitry of appetite is established in part by foods consumed during early development[30-31] and food preferences can be learned via breast-milk.[33] Nonetheless, while evidence exists for considerable adaptability early, the plasticity of these pathways diminishes over the course of development.[34-35] Therefore the period of breastfeeding, by shaping healthy food preferences and healthy growth trajectories, is a potentially critical period for combating future obesity and dealing with our changing environments. Lifestyle modifications in adulthood, once neurobiological and metabolic pathways are well-established, are likely to have a much smaller and more transient effect on phenotype.

Conclusions

An evolutionary perspective enhances our understanding of the complex interactions between food and consumers over time and thusly informs how we approach food and human health today. It is important to emphasize that not only is the genetic makeup of each individual unique, but that the genome has evolved such that many genes *depend* on environmental input in order to function. And because each individual's social, nutritional, and microbial environment is unique, the dynamic integration of their genes and environment will profit from highly personalized nutrition and medicine for optimizing human health. By gaining control of personal diets, particularly during critical developmental windows when plasticity is most evident, many dimensions of the human phenotype can be enhanced. We can therefore empower consumers to not merely perceive their health as the absence of disease, but rather the enhancement of their health, performance, and recovery throughout life.

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