


Evolutionary mismatch and modern diseases

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Abstract

The current prevalence of chronic noncommunicable diseases (NCDs) - such as autoimmune diseases, metabolic disorders, and circadian rhythm disorders - stands in sharp contrast to the health profiles of Paleolithic populations. This study examines chronic diseases through the Evolutionary Mismatch Framework, which posits that the human organism is genetically and neurobiologically optimized for Paleolithic environmental conditions, yet must function in radically altered modern contexts. The analysis focuses on three central mismatch mechanisms. The work argues that these diseases do not represent malfunctions, but rather rational responses of an organism functioning under different conditions. Implications for prevention and intervention are discussed, with a focus on hormesis and the biological reconstruction of Paleolithic environmental factors in the modern context.

Keywords: evolutionary mismatch, chronic diseases, autoimmune diseases, circadian rhythms, circadian desynchronization, Paleolithic diet, hormesis, environmental mismatches, neoantigens

1. Introduction

Since the pace of evolution cannot keep up with our rapid development, our ability to adapt to the challenges of the modern world lags behind, resulting in us suffering from chronic, non-communicable diseases more frequently than our Paleolithic ancestors. This includes, for example, autoimmune diseases, musculoskeletal disorders, and dental caries.

Nature has created a true masterpiece with the human body. Its ancestral cells are over 3.8 billion years old, and its nervous system over 500 million years. We must keep in mind that humans have spent 99% of their existence under pre-agricultural conditions. It is therefore not surprising that humans are much better adapted to the conditions of the Paleolithic era.

The human body is like an old «warrior» - over an extremely long period of time, it has learned to withstand the adversities of nature. Given this legacy, one would expect that it should not actually suffer from many of the chronic diseases that are so prevalent today.

2. Evolutionary Mismatch: Theoretical Framework

Similar framework was discussed as early as 1985 in the New England Journal of Medicine in research by Eaton and Konner.

In their groundbreaking paper “Paleolithic Nutrition: A Consideration of Its Nature and Current Implications,” the authors demonstrate that modern humans are genetically nearly identical to their ancestors from 40,000 years ago. The authors document that hunter-gatherer populations were virtually free of the chronic, non-communicable diseases prevalent today, such as diabetes, heart disease, and cancer.

This supports the notion that the human body has been programmed over millions of years for optimal health under Paleolithic conditions, and that modern chronic diseases are primarily triggered by the discrepancy between our evolutionary adaptation and the modern lifestyle.

Most people cannot imagine the incredible feats our bodies are capable of. Our bodies are naturally accustomed to swimming in freezing water, sleeping in harsh temperatures, and working under the blazing sun without immediately suffering from heatstroke. These are the conditions under which our ancestors lived and to which we have evolved. This does not mean that Paleolithic hunters and gatherers were immune, but it suggests that a lifestyle more in harmony with nature is better for our health.

Science supports this observation through the mismatch theory. Researchers like Stephen Stearns argue that many lifestyle diseases are the result of a discrepancy between our Paleolithic genome and the modern lifestyle.

3. Artificial Light and Circadian Disruption

Many of our modern inventions - essentially all interventions of the modern era - are far ahead of evolution. Especially with the electrical revolution and the invention of artificial light, we have gained such a head start that chronic diseases have become inevitable.

Our bodies interpret every light as sunlight or a fire source, and the nervous system often responds inappropriately as a result.

*The evolutionary misinterpretation of artificial light by our visual system was comprehensively documented by Czeisler et al. (2013) in the journal *Nature*. The Harvard researchers demonstrated that blue light with wavelengths around 480 nm activates melatonin suppression up to five times more strongly than long-wavelength light.*

In their study, they demonstrated that modern LED lighting with a high blue component massively disrupts the human circadian system, as our photoreceptor system (intrinsically photosensitive retinal ganglion cells) has been calibrated to natural light sources over millions of years.

The researchers demonstrated that incandescent bulbs, with their warm spectrum (2700K), have little effect on melatonin production, while LEDs at 6500K cause suppression of up to 90% - the body mistakenly interprets them as daylight.

If one were to describe this process in computer terms, one could say that modern stimuli lead to »bugs« because the body hasn't received the update for the new era and is still running on the old operating system. Even though the human body cannot be compared to a computer, the practical comparison is still a good visual reference point.

LED light keeps us awake because it contains a high proportion of blue light, similar to sunlight. The body therefore interprets LED lighting as sunlight and releases hormones that are actually intended for daytime use. The reason this doesn't happen with old incandescent bulbs is simply that they don't emit blue light, and the body interprets them as sources of fire - which were common at night during the Paleolithic era.

This is one of the reasons why, for example, blue light filters for screens are recommended to avoid disrupting sleep rhythms. The other solution to the problem, however, would be to simply not turn on artificial light at all - at least during the day - which is, however, rather unthinkable for many in the modern world.

Yet artificial light also has definite positive effects on health; when used properly, it can support natural circadian rhythms and compensate for health deficits caused by reduced exposure to daylight.

Studies show that LEDs with intensities of 2,500–10,000 lux precisely mimic the natural daylight spectrum and can thus significantly improve melatonin regulation, sleep quality, and cognitive performance in office workers. Daylight lamps with LED technology, in particular, have proven to be an effective solution to the evolutionarily unnatural lack of light in modern indoor spaces.

Despite all the artificial light, modern autoimmune diseases are a particular thorn in our side. No other human disease signals so clearly that it may simply be a reaction to foreign substances to which we are not evolutionarily adapted.

4. Autoimmune Diseases: A Misdirected Response of Prehistoric Adaptation

The natural immune system ensures that the body recognizes components that are foreign to it and eliminates them before they can cause further damage. In an autoimmune disease, the body's own immune system mistakenly attacks the body's own cells or tissues because it recognizes them as foreign. This attack leads to inflammation, tissue damage, and dysfunction of the affected organs.

But what if this reaction isn't a mistake?

It can be argued that modern humans are exposed to far more unnatural substances and stimuli than our Paleolithic ancestors. This exposure to modern stimuli (the «autoimmune triggers»), to which humans in the Paleolithic era were not exposed, can cause problems in modern humans.

The immune system is, in its own way, very intelligent and quite capable of distinguishing between a natural particle and a synthetic variant. Generally speaking, the body recognizes the natural variant because it has been exposed to it for a long time. The synthetic variant, however, represents a new exposure that is foreign to the body and, as mentioned above, can become a trigger.

4.1 Haptenization and Immune System Disruption

For example, inhaling perfume can increase the risk of developing an autoimmune lung disease. Not because perfume is toxic in itself, but because it contains synthetic fragrances that the body does not (yet) recognize in this form. The human body's initial reaction to an unknown substance or particle, such as these fragrances, is an immune response or a psychosomatic reaction - depending on the individual's state of health. The outcome can be harmless or lead to an autoimmune disease in the long term.

The observation regarding perfume can be scientifically explained by the concept of haptenization. Small chemical molecules (xenobiotics), which would be harmless on their own, bind to the body's own proteins. The immune system

recognizes this new “complex” as foreign. Studies by Aristo Vojdani (Journal of Applied Toxicology) show that such compounds can disrupt the immune system’s self-tolerance and trigger autoimmune reactions (e.g., against the thyroid or lungs).

When the body is exposed to a multitude of such «altered substances» from a wide variety of sources (including something as seemingly insignificant as drinking water that does not match the type of water - think spring water - to which the body originally adapted), the body increasingly shifts into a defensive mode.

It is often not a single substance or a single exposure that leads to measurable damage, but rather the sum of all these small, unnoticed stimuli that can lead to an autoimmune disease. For science and medicine, it is then no longer possible to identify the cause of the disease because it has been lost in a sea of these small causes.

4.2 The Exposome: Cumulative Environmental Burden

Another important concept discussed in modern research is the “exposome.” The exposome describes the totality of all environmental influences to which an individual is exposed over the course of a lifetime. A study by Wild (2005) posits that it is not the expression of isolated genes, but rather the cumulative burden of environmental toxins, radiation, and diet (precisely that “sea of causes” mentioned above) that is responsible for up to 70–90% of chronic diseases.

The point here is not to demonize the components and lifestyle of our modern age. For even the perfume highlighted here, for example, has been shown to trigger positive psychophysiological effects. Studies demonstrate that certain perfume components can modulate the autonomic nervous system, reduce stress hormones, and improve mood.

So the question isn't whether something is harmful in the context of history, but rather how to find a new way of dealing with all these inventions and innovations in order to mitigate the harmful side effects of life in the 21st century.

4.3 Stone Age reaction: The Trigger Hypothesis in Autoimmune Disease

It is certainly not possible - nor desirable - to return to the Paleolithic era to eradicate chronic diseases. Our modern inventions, such as LEDs, synthetic vitamins, and even perfume, are not a problem but a blessing. However, it would fundamentally benefit our health if we listened more closely to the body’s messages and perhaps adjusted our lifestyle slightly, rather than trying to «defeat» every symptom with medication. For medication works even better and with fewer side effects precisely

when it is in harmony with the body's nature, rather than overriding its ancient mechanisms.

The body communicates in various ways, whether through the subconscious, through psychosomatic reactions, or, in the worst case, through illness when previous attempts at communication have failed. If we listen to our bodies and take into account the stresses we face daily, we may be able to figure out how to avoid the unfortunate burdens of modern life.

To work in harmony with our bodies, which are still synchronized with the conditions of a different era, a new strategy may be necessary. Especially in the case of autoimmune diseases, the question arises as to whether it might not be more helpful to interpret the body's act of attacking its own cells as a sign that the body is being irritated by something and put on alert, which in turn forces it to launch a counterattack. And that it could therefore be quite helpful to identify this stimulus - and, if possible, to reduce it.

The trigger can be one or more «triggers» and if such triggers persist over a long period and may even lead to biological changes, an autoimmune reaction by the body is understandable. As long as these triggers exist, the autoimmune disease would continue. Therefore, it is important that potential triggers be investigated.

For example, a home with too many chemical molecules in its materials, or a job where one is exposed to excessive electronic radiation, can be a strong trigger. It may sound as though causes like these are too harmless to be co-triggers of an autoimmune disease, but the impact of such exposure should not be underestimated. Even minor deviations from what the body has evolved to adapt to can have negative effects. An abstract example would be the way olives are consumed. Whether we eat whole olives or consume industrially processed olive oil can have an impact, since the body is not accustomed to refined, pure oil. For instance, it has been observed that a patient with heartburn experienced heartburn when consuming refined oil, but not when eating many olives.

One could argue that autoimmune diseases represent an evolutionary mismatch in which modern environmental factors prompt our immune system to mount responses that were adaptive in the context of our ancestors but are harmful today. From an evolutionary perspective, autoimmune reactions could represent ancient adaptive mechanisms that have become maladaptive in the modern world.

This evolutionary discrepancy between our Paleolithic-adapted immune system and modern environmental conditions could explain why certain autoimmune reactions occur frequently despite their obvious harmfulness to the host organism.

If we assume that the body functions as intended and makes no mistakes, and that its functioning is adapted to the Stone Age - then the «Stone Age reaction» makes sense: The body defends itself against what it perceives as a threat because it has not yet adapted to modern stresses.

If one were to ask the cells why they attack their own body, they would either say that their behavior was correct at that moment - in accordance with the Stone Age reaction theory - or that, due to a lack of adaptation, they did not know how else to react.

The rising prevalence of many of today's chronic diseases supports this theory. Whether it's diabetes or osteoporosis, they all have one thing in common: the strongest risk factors are those that didn't even exist in the Stone Age, such as a lack of exercise or an unhealthy diet.

5. From Disease to Adaptation: Restoring Harmony with Our Nature

5.1 The Infallibility of Nature

There is no concrete reason in nature to assume outright that the body mistakenly attacks its own cells. Autoimmune diseases exhibit clear patterns that point to more than just a malfunction. The systematic patterns and the increasing prevalence of autoimmune diseases in modern societies suggest that these may not be random errors, but rather misguided reactions to unknown triggers.

The dramatic rise in chronic diseases over the course of just a few decades does not point to evolutionary errors, but rather to the fact that human bodies are still functioning according to ancient programs in an environment for which they have not yet been optimized. Evolution does not produce widespread systematic errors within a few generations.

5.2 Aligning Modern Health with Paleolithic Conditions

As a society, we are - at least on the whole - fairly united in our views on what we consider healthy. If, for example, a healthy diet or exercise is scientifically recognized to reduce or even eliminate the risk of chronic diseases, this reflects conditions more typical of ancient times than of the present.

A diet rich in omega-3 fatty acids, protein, and vegetables is healthy insofar as it more closely resembles the diet Paleolithic humans were accustomed to. Back then, when we still had to hunt and gather, our food consisted mainly of animal meat and vegetables. Stone Age animals, much like today's wild animals, contained more omega-3 than omega-6 fats compared to our modern domesticated animals.

Randomized controlled trials (RCTs) show that a Mediterranean diet rich in omega-3 fats, fruits, vegetables, and lean protein can reduce the risk of autoimmune diseases by up to 30% (Kumar et al., 2021). This diet more closely aligns with the dietary conditions of prehistoric humans and supports natural immune regulation.

Refined sugar also owes its unhealthy reputation to the fact that it is incompatible with modern life. After all, in the Paleolithic era, the only source of sugar was fruit. Fruit was scarce and, moreover, seasonal. Even today, the brain rewards us for sugar because it always assumes we are eating fruit - at least, the brain does not recognize industrially produced forms of sugar. Combined with the fact that we consume sugar too easily and too often today, this has led us humans into an excessive sugar rush. As a result, the majority of humanity consumes far too much sugar, and society is struggling to break free from it. The dopamine system, which was originally meant to keep us alive, now literally forces us to harm ourselves. In this regard, we remain puppets of nature, misusing resources out of sync with the times to which our bodies have adapted.

Another key element of our health today is exercise and sports. This is no coincidence; it is demanded of us because the body is accustomed to being constantly in motion.

We don't have to go jogging because it's healthy. We have to move because the heart is accustomed to it. Our ancestors ran a tremendous amount; their everyday pace was, in part, what we would call jogging today. So when we move, we bring the body back to where it belongs: to another time.

Now we have the privilege of not having to go jogging and of being able to more or less do without a healthy diet. But there is no question that in doing so, we also curb its ability to successfully resist pathogens. We thus lock the »mighty warrior of evolution« into a modern cage, which then responds to us with disease.

6. Conclusion

Consequently, chronic diseases can often be caused by mistreating our bodies, and are not always a random reaction of nature. The perfect masterpiece - the human being - thus becomes an overwhelmed creature that expends all its resilience to resist new and unfamiliar stimuli.

The restoration of hormesis - the body's ability to build resilience through natural stimuli (cold, heat, fasting, exercise) - should not be underestimated. Modern research on longevity shows that it is precisely these "Stone Age stimuli" that activate certain longevity genes, such as sirtuins. In this sense, healing does not mean suppressing symptoms, but rather the biological reconstruction of the living conditions for which our bodies are optimized - only in the 21st century.

When we consider this, we can come to the realization that diseases are not necessarily the body's misreactions, but rather potential errors that we create by ignoring its nature.

We need not forego the luxuries of modern times, nor do we have to give up our sugar addiction; however, we must find a new way of dealing with the consequences that result from them - above all, to prevent chronic diseases.

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