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Evolutionary Medicine: The Impact of Evolutionary Theory on Research, Prevention, and Practice

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ABSTRACT

We review recent evidence for a growing number of discrepancies between our contemporary existence and evolutionary history which have the potential to impair and undermine features of human mental and physical health. Included in this review are health issues related to bottle feeding, caesarian section, infection, cleanliness, fever, exercise, diet, mate choice, contraception, semen sampling, and body odor suppression.

KEYWORDS

Postpartum Depression, Asthma, Autism, Immune Function, Mate Choice, Reproductive Outcomes

INTRODUCTION

Evolution is a gradual, incremental process operating over extended periods of time often measured in thousands or even millions of years. Unlike other life forms, the human species has managed to produce a variety of recent technological changes that have the potential to radically alter our environment and emancipate us from some of the conditions that gave rise to our existence. Although the impetus for some of these changes date back thousands of years (e.g., modifying pieces of stone to produce primitive tools), these technological developments have been increasing at an exponential rate over the past several hundred years. As a consequence, we have reached the point where some of these technological developments have outstripped our evolutionary capacity to keep pace and this is having adverse medical and psychological consequences.

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Evolutionary medicine is an attempt to identify and resolve some of these counterproductive mismatches between our evolved adaptations and different aspects of our contemporary existence. To illustrate the emerging discipline of evolutionary medicine, we selectively focus in this paper on a number of recent technological developments that have begun to undermine and interfere with our physical and/or psychological wellbeing.

BOTTLE FEEDING AND POSTPARTUM DEPRESSION

One of the defining features of the mammalian order, of which we are only one of over 3,000 species, is the capacity to produce milk to feed relatively helpless, parent dependent offspring. For most of human evolutionary history there were no alternatives to breastfeeding, and a decision not to breast feed would have been tantamount to committing infanticide. However, within the last hundred years the technology has emerged that now makes bottle-feeding an alternative to breastfeeding. As a consequence, women who lack the capacity to produce adequate breast milk or have to leave home to return to work often exercise the option of bottle-feeding their babies.

Bottle-feeding is a classic example of a technological development that has put us out of phase with our evolutionary past. Not only is formula a poor substitute for breast milk and may compromise the health of the infant (Heining & Dewey, 1996), but mothers who bottle feed may also be putting themselves at risk. For instance, the risk of becoming overweight (Chapman, 2009) as well as the risk of developing breast cancer (Stuebe, Willert, Xue, & Michels, 2009) is significantly higher among mothers who bottle-feed rather than breastfeed their infants.

For most of human evolutionary history the absence or sudden cessation of breastfeeding would have been occasioned by stillbirth or neonatal death, and therefore bottle feeding may unwittingly simulate child loss (Gallup, Pipitone, Carrone & Leadholm, 2010). Consistent with this hypothesis, the death of a child is a powerful trigger for depression (Suarez & Gallup, 1985), and there is growing evidence that bottle-feeding is a significant risk factor for postpartum depression. To make matters worse, women with postpartum depression who are treated with antidepressants are sometimes advised to discontinue breastfeeding because the medication may get into the mother's milk. Other hospital practices may also unwittingly simulate child loss, such as subjecting mothers to periods of separation from their infants as a result of keeping newborn babies in nurseries.

For mothers who want their babies to benefit from breast milk but have to return to work following the birth of a child, expressing breast milk that can be fed to the child by a caretaker with a bottle is a commonly employed option. In such instances, we would recommend mothers videotape breastfeeding episodes with their baby for playback while expressing milk at work, as a means of simulating breastfeeding and maintaining their bond with the baby to minimizing features of child loss.

BOTTLE FEEDING AND AUTISM

Not only does bottle-feeding create conditions that used to be associated with the death of an infant, bottle-feeding undermines natural birth spacing mechanisms. Breastfeeding produces hormonal changes that serve to promote lactational amenorrhea and anovulation. Both of these conditions evolved to reduce the likelihood of re-impregnation during the postpartum period and function to promote birth spacing. Pregnancy and lactation are very biologically and metabolically expensive, and therefore being re-impregnated while still nursing a young infant could seriously compromise the quality and quantity of milk for the existing child, as well as diminish the nutritional status of the prenatal environment for the developing fetus.

A recent paper in the journal *Pediatrics* (Cheslack-Postava, Liu & Bearman, 2011) reports that children conceived within a year of their next oldest sibling are three times more likely to develop autism, and those conceived within two years of their next oldest sibling are twice as likely to develop autism. We've argued that these peculiar birth order effects on the risk of autism may be a consequence of nutritional deficiencies in the prenatal environment that occur as a result of closely spaced pregnancies due to bottle feeding (Gallup & Hobbs, 2011). In other words, by disrupting natural birth spacing mechanisms the decision to bottle-feed your last child may make re-impregnation more likely during the postpartum period, and increase the risk of autism in your next child.

Research by Ronald et al. (2006), showing a high degree of concordance in the incidence of autism among both identical and fraternal twins, is consistent with this interpretation of birth spacing effects on the risk of autism based on prenatal environment deficiencies.

CAESARIAN SECTIONS AND ASTHMA

In much the same way that bottle feeding puts the mother out of phase with her evolutionary history, caesarian sections also preclude important aspects of the normal birth process. Caesarian sections were not an option during 99% of evolutionary history. Women who were incapable of delivering a child due to constraints on the size of the birth canal or other complications (such as a breech birth), would have died along with their unborn children.

Babies delivered nowadays by caesarian section not only have lower Apgar scores (as a measure of the infant's health and vitality), but they are at a higher risk of neonatal respiratory distress. These respiratory problems appear to be a consequence of the retention of amniotic fluid in the lungs that would otherwise have been purged from the lungs due to the compression that occurs during a normal vaginal delivery.

In later life, children delivered by caesarian section are also more likely to develop asthma. The connection between asthma and caesarian section appears to be due to the early absence of critical bacterial flora in the child's intestinal tract that promotes healthy immune system development (e.g., Azad et al., 2013). During a normal delivery, the baby is exposed to and ingests bacteria in the mother's vagina that serve to colonize critical parts of the infant's digestive tract,

which in turn stimulate the baby's immune system. The intestinal flora of babies that are bottle-fed also lack certain beneficial bacteria, suggesting that the skin around the mother's nipples contain bacteria that colonize the baby's intestinal tract as well. To make matters worse, women with caesarian sections sometimes delay breastfeeding or opt not to breastfeed at all. Moreover, mothers who undergo caesarian sections may be treated with antibiotics prior to surgery to minimize infections, which can have the unintended consequence of destroying many of these beneficial bacteria and interfering with the colonization process.

An obvious way to reinstate this natural immunization process in caesarian section babies would be to routinely harvest bacteria from the mother's vagina with a sponge, so that the baby could be bathed in the mother's vaginal fluid after delivery as an alternative means of initiating this colonization process.

SITES OF INFECTIONS

The skin is an important line of defense against infection. The easiest entry sites for infection are at the superficial level; cuts, scrapes, and scratches, typical innocuous injuries which create a pathway for microbes to enter the body. It is not surprising therefore that one of the most vital components of the human immune system is embedded immediately beneath the skin.

Recent research has shown that certain vaccinations administered at the subcutaneous level by scratching the skin are more effective than injecting vaccine into deep muscle tissue (Jiang et al., 2012). In fact, both circulating and skin T-cells are generated after skin infection. Having only circulating T-cells is not as effective for viral clearance, thus skin T-cells are superior when it comes to protection. In light of this evidence, novel methods of vaccination could be explored to increase effectiveness.

In the ancestral environment, humans were subjected to a wide variety of circumstances in which cuts and scrapes were common. It can be argued that exposure to viruses and various other microbes through these entry points tended to promote immune system function. Many of us are now removed from conditions where cuts and abrasions are a part of the norm, thus making ourselves more vulnerable to infections that may otherwise be tolerated. Furthermore, it is common practice to apply an antibiotic ointment immediately after such an injury, thus limiting exposure and perhaps doing ourselves a disservice, particularly during development.

CLEANLINESS

It has long been thought, and recent evidence supports the notion that the mammalian host is most sensitive to initial exposure of microbes during neonatal life (Olszak et al., 2012). In modern society, where cleanliness is viewed as next to Godliness, it is common practice to protect children from dirt and germs. Although hand-washing is one of the most important prophylactic measures in medicine, it may be counter-productive to prevent children from getting "down and dirty" and being exposed to many common germs.

A healthy immune system requires challenges, as evidenced by vaccinations. Children who are raised in protected, relatively germ-free environments, have inferior, compromised immune systems and are susceptible to autoimmune diseases (Olszak et al., 2012). The lungs and colon are sites where microbial contact is common. Research shows that asthma and inflammatory bowel disease, both immune mediated conditions, are more common in humans who have not had early-life microbial exposure. Other things being equal, exposing children to germs that will challenge their immune system should lead to greater overall health.

Certainly, the Environment of Evolutionary Adaptedness (EEA) provided the conditions for such challenges. In a time when hypoallergenic pillows, antibiotics, and hand soap didn't exist, germs were still ubiquitous. There were numerous threats that faced a new-born, and it is likely that many did not survive into adulthood. However, the evidence shows that these children may have had a better chance of warding off infection than modern children. Therefore, keeping kids protected in an artificial environment is ironically detrimental to their health. Again, we see that the consequences of removing ourselves from a habitat that gave rise to our existence can be counterproductive. This very simple notion is absent in much of medical practice, where the treatment of symptoms is a primary objective, and prevention is often secondary.

FEVER

A paper in the journal *Surgical Infections* (Schulman et al., 2005), dispels the paradigm of antipyretic therapy (treating fever) commonly employed for critically ill patients with fever, by reporting an increase in morbidity and infection in subjects who underwent aggressive treatment as compared to those who voluntarily did not. In extreme cases, fever can be fatal. However, a low-grade fever is often beneficial and acts as an evolved defense mechanism for fighting infection. With the advent of pharmacological interventions such as acetaminophen and cooling blankets, we are preventing the body from carrying out a natural convalescent function. Furthermore, these interventions can have deleterious side effects such as liver damage and may also lead to adverse interactions with other medications. The upshot of symptom relief is a suppression of anti-body and cytokine production, and the release from inhibition of microbial growth.

The rationale of antipyretic therapy is largely unfounded. The common justification of such measures include: the comfort of the patient, lower cardiovascular stress and an avoidance of increased oxygen consumption (Schulman et al., 2005). There is, however, a lack of evidence to support the use of antipyretic therapy for these indications. Medical practice and research could benefit from seeing this condition through an evolutionary lens. Infections being a mainstay of life, it stands to reason that evolution would select for a biological function that promotes the elimination of such a threat. When it comes to fever, physicians may want to employ a counter-intuitive, but simple philosophy of "don't just do something, stand there."

IMPORTANCE OF EXERCISE AND DIET

For most of human evolution, frequent and intense physical activity was an essential feature of life because of the rigors of survival. Hunting, gathering food, finding water, evading predators, and building shelter was undoubtedly a time consuming and taxing process. Drought, illness, failed hunts, and a variety of other issues would often interfere with the ability to collect food. Individuals were more likely to survive periods without food if they had genes that provided for efficient conservation of glycogen and depositing/storing fat during times when food was plentiful (Chakravarthy & Booth, 2004). Under these conditions, individuals were selected for their ability to effectively cycle between physical activity and rest, as well as between feast and famine. However, aspects of Western society have replaced the need for physical activity and the occurrence and duration of famine is far less frequent. As a result of mechanization and modern agriculture, individuals now have access to large amounts of processed food with little activity or exertion needed to obtain it. On a daily basis, it is estimated that individuals with sedentary lifestyles use 1,200 less calories than hunter-gatherers (Chakravarthy & Booth, 2004). Technology has also brought about greater opportunities for leisure, such as television and artificial lighting, which contribute to inactivity and overeating. Pairing inactivity with diets containing excessive amounts of fat and a variety of foods our bodies haven't evolved to process, has put us out of phase with the lion's share of our evolutionary history and has proven hazardous to our health.

Artificial illumination has made it possible for humans to stay awake long after the sun has set, making sleep deprivation a common phenomenon. Sleep deprivation increases hunger and appetite (Siervo, Wells & Cizza, 2009). Fatigue caused by sleep deprivation may also decrease motivation to exercise. Light plays an important role in the circadian clock that regulates the timing of eating and sleeping. Low levels of light present during the night are enough to disrupt the circadian rhythm. This disrupts metabolism and feeding behaviors and may result in excessive weight gain (Fonken et al., 2010).

Other types of technology driven by an emphasis on leisure and entertainment, such as computers and television, provide people with distractions while they eat. These distractions can also interfere with neural satiety signals and result in increased food intake (Siervo et al., 2009). Many food advertisements alter emotional responses to food and are designed to increase its reward value, exacerbating cravings. Often typical work environments are associated with chronic stress caused by a lack of power and a low reward/effort ratio. Chronic stress has also been shown to increase the reward value of food, which can lead to overeating and obesity (Siervo et al., 2009). Nowadays food is easily accessible and many individuals are able to indulge in their increased desire to eat. Modern technology in the Western World has created the equivalent of a continuous feast. Human digestion and metabolism did not evolve to deal with chronic overeating.

The agricultural revolution has further changed human eating habits by introducing saturated fats, cereal grains, and large amounts of sugar and salt into the modern diet. Our ancestors rarely, if ever, encountered such foods. It is problematic that many individuals today rely on these foods as a main source of nutrition. Not only are they a poor source of fiber and vitamins, many also contain

high concentrations of saturated fat. Meat harvested from domestic animals has about six times more saturated fat than meat from wild game (Chauveau, Fouque, Combe & Aparicio, 2013). Diets high in saturated fat are associated with impairments in episodic memory, attention, and inhibition (Francis & Stevenson, 2013). High saturated fat diets may increase the risk of developing Alzheimer's disease and Parkinson's disease (Francis & Stevenson, 2013). Diets high in cereal grains and simple sugars frequently increase inflammation and insulin sensitivity, which puts individuals at risk for Type 2 Diabetes (Jönsson et al., 2009). Various studies have found that eating lean meat, fish, nuts, eggs, fresh fruits, and vegetables while avoiding grains, dairy, and legumes leads to healthier weight, blood pressure, and cholesterol (Chauveau et al., 2013). It is advisable to eat a diet that's in sync with our evolutionary history.

Advances in industrialization have made it unnecessary for many individuals to engage in hard labor in order to procure food or build shelter. Instead, more and more people have "desk jobs" that involve sitting for long hours at a time. Physical inactivity gives rise to a variety of problems. Inactivity can cause accumulation of abdominal fat and activation of inflammation pathways that result in insulin resistance, thickened artery walls, neurodegeneration, and tumor growth (Pederson, 2009). These health issues can lead to Type 2 diabetes, cardiovascular diseases, colon cancer, breast cancer, dementia, and depression (Pederson, 2009). Hunter-gatherer societies have a much lower prevalence of these types of diseases (Chakravarthy & Booth, 2004). A sedentary lifestyle is associated with dangerous health risks. Just the amount of time spent sitting increases the risk of premature death (Patel et al., 2010), and there is growing evidence that exercise can reduce the effects of age related cognitive impairment and dementia (Heyn, Abreu & Ottenbacher, 2004).

Because the demands of survival put a premium on physical labor during our evolutionary history, it was natural that when such rare opportunities arose people would indulge in rest and relaxation to recuperate and conserve energy for the next exhausting task. However, relaxation should be taken in moderation because the effects of inactivity set in quickly. Healthy humans show prediabetic symptoms within 3 days of bed rest, and athletes show prediabetic symptoms after 10 ten days without exercising (Chakravarthy & Booth, 2004). Reducing food intake and increasing physical activity on a long-term basis can reduce the over activation of inflammation pathways. The inclusion of at least 3 hours of moderate exercise per week leads to a 30% reduction in stroke, Type 2 diabetes, and heart disease (Chakravarthy & Booth, 2004).

MATE CHOICE

Humans have created an environment in which natural mate choice mechanisms may not always operate effectively or appropriately. Hormonal contraceptives (e.g., birth control pills), condoms, and body odor suppression strategies are three contemporary practices that may undermine informed mate choices. By restricting the exchange of biological information, feelings of attraction may not be driven by evolved mechanisms that take into account actual health cues

or compatibility signals, which can in turn lead to less than optimal, imperfect mate choices.

Hormonal Contraceptives

While hormonal contraception is an effective means of reducing the risk of unwanted pregnancy, it also eliminates natural hormonal fluctuations due to the menstrual cycle that function to promote informed mate choices and signal fertility to possible mates. A naturally cycling female experiences heightened olfactory sensitivity when she is ovulating, which activates mechanisms that enable her to unwittingly gauge the MHC compatibility of a potential mate, as well as body odor cues that signal important variation in a male's fluctuating asymmetry. Ovulating females find the body odor of males with compatible MHC and low fluctuating asymmetry to be more attractive than that of an incompatible male (Thornhill & Gangestad, 1999).

Birth control effectively suppresses a female's ability to detect these cues during the ovulatory phase of the menstrual cycle. This poses problems in two ways. First, if she develops a pair bond with a male while on birth control, and later discontinues using hormonal contraceptives, she may find herself no longer attracted to her committed partner (Roberts et al., 2012). Secondly, if she becomes pregnant with that male, it could compromise the health and genetic viability of her offspring.

While a female's choice in mates has important consequences for her reproductive success, she must also present herself as a desirable mate in order to attract a high quality male. Hormonal contraceptives interfere with this aspect of competition for high quality males, as they lower the female's voice, face, body configuration and odor attractiveness, as well as raise her fluctuating asymmetry. They also eliminate the natural fluctuations in attractiveness during the menstrual cycle that make females appear most attractive when they are ovulating. Miller, Tybur, and Jordan (2007), for example, showed that lap dancers who use hormonal contraceptives earn significantly less than naturally cycling females who are not menstruating. Furthermore, hormonal contraceptives have many unintended side effects, such as a lower quality of vaginal lubrication and an increased risk of contracting STDs, due to a change in vaginal acidity. Most of these side effects are not discussed with patients before they decide to use hormonal contraceptives, and it is important to further examine such effects, as well as inform prospective users of the potential costs.

Semen Sampling

The use of condoms may also interfere with a female's assessment of mate compatibility. Much like appearance, body morphology, and odor can be used to index health, fertility, and compatibility, the chemical composition of semen may also contain cues to fitness. A particular male's unique semen signature (Davis & Gallup, 2006) contains information which might allow a female to assess the compatibility of the pairing (Gallup & Atkinson, 2012). Semen sampling was likely an inherent feature of courtship and mate choice during human evolution. A kiss between two

genetically incompatible people may lead to feelings of disengagement and lack of interest (Hughes, Harrison, & Gallup, 2007). It is possible that insemination results in the activation of parallel mechanisms that could lead to feelings of regret the next morning if the pairing was not a good match.

While condoms are effective at reducing unwanted pregnancies and STDs, they mitigate semen exposure, which prevents semen sampling and may impair informed mate choices. The advent of condoms could lead to consequences similar to hormonal contraceptives; e.g., a lack of or change in attraction if the male chooses to stop using condoms, and a higher likelihood of genetically disadvantaged offspring. If true, such information could enable people to make more informed cost-benefit analyses when deciding whether to use condoms.

Odor Suppression

There is a vast array of female cosmetic products and procedures to make women more attractive so that they appear to be more reproductively viable and have better genes. These cosmetics function to mask cues of aging and exaggerate the appearance of being reproductively viable. However, in the name of hygiene and odor suppression, females also often deodorize and remove underarm and pubic hair, which may unwittingly mask, alter, or eliminate important reproductive and mate quality odor cues. The removal of these specialized hair follicles prevents them from collecting and diffusing such cues. We may differentially perceive the attractiveness of a person's scent based on reproductively relevant information, whereas if someone smells appealing based on artificial, superimposed external odor sources, we once again may be impaired in terms of our ability to make informed mate choices. The invention of razors and deodorants is yet another way in which we have put ourselves out of phase with our evolutionary past, which leaves us in a position of having to contend with greater ambiguity when it comes to selecting a proper mate.

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