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REVIEW: Impact of Environmental Pollution and Modern Lifestyle on the Human Nervous System

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ABSTRACT

The unique characteristics of today's humans, such as their brains, are the result of millions of years of evolution in a very healthy environment. Thousands and millions of years ago, the environment was not manipulated like it is now, and the climate was not polluted by human activities like it is today. At that time, people ate organic food and enjoyed a healthy climate. Today, humans live in an industrialized world, and eating processed foods has become a part of their daily habits. Drinks and foods that have different additive compounds, alcoholic beverages, drugs/smoking, and all kinds of fast foods have changed the human diet. The consumption of fruits and vegetables grown in environments contaminated with heavy metals and various poisons and fertilizers is a major challenge in food health. Human sleep and wake cycles today are very different from those of thousands of years ago because of the presence of night lighting facilities, night jobs, and entertainment. Therefore, the lifestyle of today's man can affect his organs, sex cells, and embryonic period, and finally, he can face a serious challenge to the development of his nervous system. This type of lifestyle is associated with oxidative stress, inflammation of the brain, and various diseases of the central nervous system, such as anxiety, depression, and memory impairments. As a result, today's man, with his manipulations in the world in which he lives, causes his advanced nervous system, which results from millions of years of evolution, to face challenges.

Introduction

Approximately 7-9 million years ago, early hominins and chimpanzees were derived from a common ancestor (1). After millions of years and passing through a branched and complicated evolutionary path, modern humans (Homosapiens) finally entered the field of life between 400 and 700 thousand years ago (2), with the most evolved members (less than 200,000 years). BC) began to dominate the planet as a successful species. For thousands of years, modern humans have been taking their food from nature. Hominid ancestors, including early human species, consumed

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foods exclusively from the list of wild animals and uncultivated plants (3). Tens of thousands of years ago, Homosapiens were fed entirely organically by hunting and using plants and fruits (4). The beginning of the deep transformation of our ancestral diet was 10,000 years ago, after the inventions of agriculture and animal husbandry (5), but today, there have been extensive changes in the diet of humans and the status of hunter-gatherers in the plains of Africa, it has been replaced by fast food. The use of fast foods is increasing daily worldwide (6).

Humans who used stone and wood to make daily work tools hundreds of thousands of years ago have now turned to industry and enormous factories to meet their needs. In addition, the ever-increasing need for food and equipment along with the increase in population has led to the construction of more factories and the production of fertilizers and pesticides, which has polluted the planet's climate (7). Electrical control and the production of all kinds of lighting devices and electronic entertainment devices, such as smartphones, have drastically changed the sleep-wake cycle of today's man. Their rest and activity times are completely reversed (8). Therefore, the world in which man is present today is very different from thousands and hundreds of thousands of years ago. Today, with the advancement of technology, people's lifestyles have changed substantially, and the current environment is very different from the environment of thousands of years ago, in which human development and evolution took place. Therefore, in the present study, an attempt was made to examine the impact of current human environmental pollution and new lifestyles on the modern brain.

Air Pollution and the Human Brain

Tens of thousands of years ago, when humans were completing their evolutionary puzzle, the air was very clean and free of pollutants, and the first humans were active in a very healthy environment. However, today, the situation is very different, and the environment is polluted by all types of machines and factories (9). The quality of human air has a very important role in health (10). The suspended particles in the breathing air can reach the brain through the blood and eventually cause neurotoxicity (11). The entry of various pollutants into the air is related to a range of diseases of the nervous system in humans (12). Airborne particles stimulate alveolar macrophages, and these macrophages produce proinflammatory cytokines, which eventually enter the blood (13). Inflammatory mediators in the blood can also enter the brain (14). Pollutant particles can cause a chain of events that cause damage to the central nervous system (15). In this context, research has been conducted on laboratory animals. The results of a previous study revealed that exposure of laboratory rodents for 10 months to particles with a diameter of 2.5 micrometers in breathing air caused disorders in learning spatial memory and depression, as well as increased expression of proinflammatory cytokines in the hippocampus. In the same study, it was reported that the density of dendritic spines and dendritic branches decreased in the CA1 and CA3 regions of the hippocampus of rats, respectively (16).

With significant advances in biological sciences and the increase in public health knowledge, everyone now knows that a mother's lifestyle during pregnancy can affect her fetus (17). Exposure to airborne nanoparticles before birth can cause abnormalities in fetal neural differentiation (18). Studies have shown that prenatal exposure to diesel particles via maternal oropharyngeal aspiration increases IL-6 in the fetal brain (19). Therefore, it is not far from expected that air pollution can target DNA and cause gene mutation (20). Particulate matter and other environmental toxins alter the expression of microRNAs that play a role in regulating gene expression (21).

Polycyclic aromatic hydrocarbons (PAHs) are a group of pollutants that are usually formed in ambient air from the incomplete combustion of fossil fuels (22), and exposure to these types of pollutants induces mutations (23). Therefore, air pollution can put the human genome at risk and challenge the human genome, which has evolved for

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hundreds of thousands of years in healthy air. In addition, these contaminants can reach the fetus through the mother's blood and placenta and cause defects in the formation of organs such as the brain of the fetus (18). Finally, these defects can be transmitted to subsequent generations.

Water Pollution and the Human Brain

The life of organisms on the planet depends on water, and today, people know the importance of healthy water more than ever (24). We obtain water daily by drinking water as well as by consuming a wide range of foods and beverages (25). The quality of the food we consume is directly related to the water used to grow these products (26). Humans have lived in plains, forests, and rivers since hundreds of thousands of years ago, but in no period of history, they have polluted water as much as they currently do. Today, rivers, seas, and oceans are polluted by human activities (27). The health of marine animals such as fish, which are part of the human food chain, is endangered by destructive human activities. Human population growth and industrial and agricultural activities are the main factors of water pollution (28). Contaminated water can cause various bacterial (29) viral infections (30). Heavy metals such as lead, copper, chromium, and zinc can enter water through human activities, and these metals can ultimately enter human bodies through agricultural and livestock products and cause disease (31). Water micropollutants, which can be from different sources, have created a great challenge (32). In addition, plastics are among the factors that pollute water, and thousands of tons of plastics enter seawater every year (33). Plastics can endanger human health (34) both directly and by polluting the environment (35). Studies have shown that plastics can also cause neurotoxicity (36).

Today, millions of large and small industrial factories exist worldwide, which will likely increase due to the growth of the human population and the increasing needs of industry. Industrial wastewater is another factor of water pollution that can reach the human food chain in different ways and ultimately cause various diseases (37). Chemicals, oils, drugs (38), heavy metals (39), and phenol and phenolic compounds are components of industrial wastewater (40). The results of studies have shown that pollutants in drinking water, such as nitrate and nitrite, are among the causes of gastrointestinal cancers (41). The quality of drinking water is very important for the proper functioning of the nervous system (42) and water pollution can cause disorders in the human nervous system. The role of heavy metals such as lead (43), aluminum, and copper (44) in drinking water has been proven in the development of Alzheimer's disease. An increase in the incidence of brain tumors associated with polluted water has been observed in industrialized countries (45). Lead can pass through the blood-brain barrier, so it can travel to different areas of the brain and cause a variety of neurological disorders, such as mental retardation, Alzheimer's disease, Parkinson's disease, and schizophrenia (46). Environmental lead exposure increases the expression of genes associated with neurological disorders. Arsenic and fluoride are also major water pollutants. Consumption of drinking water contaminated with arsenic (47) and fluoride (48) can lead to neurotoxicity. Moreover, arsenic can cause genotoxicity (49). Therefore, pollutants in water can cause genetic damage. Genotoxic effects in fish are generally related to the content of heavy metals in water samples (50).

In recent decades, the use of pesticides has increased. In addition to the beneficial effects that pesticides have, they also have negative effects (51). Pesticides can cause water pollution (52) and thus disease in humans, and neurotoxicity is one of the reported types of damage caused by pesticides (53). Several pesticides, such as organophosphates, carbamates, and organochlorine pesticides, directly target nervous tissue as a mechanism of toxicity (54). The prevalence rate of some types of cancer, including brain cancer, is significantly higher in populations in areas where pesticides are used more than in other areas (55). Cholinesterase inhibitors are a group of insecticide chemicals that include

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some of the most toxic chemicals known to humans. Among these inhibitors are organophosphates and N-methylcarbamate, which inhibit the acetylcholinesterase enzyme and lead to excessive nerve stimulation (56, 57). DDT and dieldrin are two types of organochlorine insecticides that cause neurotoxicity and cognitive deficits (58). Moreover, Pesticides can be among the factors involved in the development of central nervous system diseases, such as Parkinson's disease, and high levels of dieldrin in the brains of Parkinson's disease patients after death have been observed (59). In addition, exposure to pesticides can also cause Alzheimer's disease (60). Therefore, exposure to pesticides either directly or through food can cause problems in the nervous system.

The exposure of pregnant mothers to water pollution due to pesticides can cause cancer in their babies (61). Exposure to pesticides can harm the nervous system. Some pesticides may affect the fetus in utero, suggesting potential harm from maternal exposure to pesticides (62, 63). Organophosphate pesticides have negative effects on the nervous system of fetuses in the womb. The results of these studies indicate that pesticides cause mutations (64). If pesticide exposure occurs before conception, it causes epigenetic alterations in gene expression and DNA methylation in parental gametes. It affects DNA imprinting and methylation in the parent's gametes (65). As a result, drinking water contaminated with pesticides can damage the brain and can also have destructive effects on the nervous system of fetuses. Therefore, they can challenge the nervous system of successive human generations. Therefore, any type of pollution in water of any origin, including industrial, agricultural, and domestic sewage, can ultimately cause water toxicity, and by contaminating human food or drinking water, it can damage the human body. During the last century, due to the increase in the world population, the need for chemical fertilizers has increased to produce more crops and provide food (66). Finally, fertilizers and pesticides can enter the human body through water and food. Direct human exposure to pesticides such as organic pesticides occurs through contaminated fruits, vegetables, grains, dairy products, and meat, as well as through agricultural environments (67).

Global Warming and the Human Brain

Today, as a result of destructive human activities, the temperature of the Earth has increased. Among the human activities that cause global warming are the burning of fossil fuels (coal, oil, and gas) and large-scale deforestation, which cause the release of large amounts of greenhouse gases such as carbon dioxide into the atmosphere. Global warming is the most important environmental problem in the world (68) because of its negative effects on human societies (including a significant increase in sea levels) and ecosystems. Global warming can endanger human health (69). One of the ways through which global warming can endanger human health is the increase in infectious diseases common to humans caused by animal vectors (70), and the increase in the population of disease-causing insects such as mosquitoes (71), which cause a range of diseases, including central nervous system diseases such as encephalitis. In addition, global warming can cause the spread of pathogenic viruses (72) and bacteria (73), and these microorganisms also cause various diseases of the nervous system (74). In addition to the indirect effects of global warming on the brain, it is possible that global warming can cause dozens of types of damage to the brain (75).

Diet and the Human Brain

Today's diet has many differences from the diets of intelligent people thousands and hundreds of thousands of years ago. Hundreds of thousands of years ago, humans used only organic seeds, fruits, plants, and meats (76). Approximately 200 years ago, the human diet changed significantly, and white crystalline sugar (glucose) was introduced into the diet (77). Glucose causes the accumulation of fat tissue by increasing the level of insulin in the body, which is an anabolic hormone responsible for the distribution of energy in the body (78). The prevalence of obesity is

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one of the side effects of changing a healthy diet and increasing the consumption of sugar and sweets (79). With increased glucose consumption and increased insulin over several years, insulin resistance (type 2 diabetes) begins more quickly or later (80). Insulin resistance in the brain plays an important role in the development of Alzheimer's disease (type 3 diabetes) (81). The insulin signaling pathway, which is essential for cell growth, repair, and energy homeostasis, is disrupted in type 3 diabetes, and a lack of insulin response is observed in the central nervous system. This incomplete insulin function in the brain leads to neurodegeneration and cognitive dysfunctions and ultimately leads to Alzheimer's disease (82). Furthermore, insulin resistance in the brain is associated with mitochondrial dysfunction, oxidative stress, and glutamate toxicity, all of which contribute to insulin insensitivity in neurons (83). Increased insulin levels have significant physiological effects on reproductive organs in men and women (84). In men, insulin hormone signaling disorders caused by diabetes can lead to morphological and functional changes in sperm and affect spermatogenesis, testicular function, and testosterone synthesis (85). On the other hand, in women, high levels of insulin, as observed in conditions such as polycystic ovaries and type 2 diabetes, can disrupt ovarian function and lead to menstrual dysfunction, anovulation, infertility, and an increased risk of miscarriage (86). Maternal hyperglycemia during pregnancy resulting from exposure of the fetus to high levels of glucose significantly affects the growth and development of the fetus and leads to fetal hyperglycemia and hyperinsulinemia. This exposure can lead to altered developmental pathways, impaired neural and cardiac development, and premature pancreatic exhaustion in the fetus, increasing the risk of metabolic diseases later in life (87).

Fifty years ago, the consumption of processed and ultra-processed foods such as fast food and processed drinks began and has increased worldwide (88). These changes in diet have been associated with many types of harm (89). These types of foods can cause negative effects on cerebral vessels and, as a result, can affect brain energy (90). An unhealthy diet can affect the brain during the sensitive period of adolescence and have negative effects on the development of the nervous system (91). An unhealthy diet, such as fast food, can cause the genetic inheritance of nervous system diseases through parental gametes (92) through its effects on gene expression (93).

Advances in biological science have made it possible for humans to manipulate genetics to achieve goals such as producing more efficient plants and animals. Genetically modified organisms, also known as transgenic organisms, which are used as human or animal feed, are common today and have entered the food chain (94). There are specific concerns about these foods. The effects of these types of foods are not fully understood (95). However, of greatest concern is the activation of silenced or underexpressed genes. This is because it is possible to activate genes that encode enzymes in biochemical pathways, leading to the production of toxic secondary compounds (94). Genetic modification can lead to an increase in the level of toxins in plant foods and cause risks to consumers of these products (96). Although there is not much information about the possible negative effects of these foods on human health, investigating the effects of these foods on the health and structure of the human nervous system is highly important.

Drug/Alcohol Use and the Human Brain

The consumption of alcoholic beverages also has negative effects on the nervous system. Alcohol consumption is widely associated with cell death, including apoptosis, necrosis, and autophagy. Alcohol-induced cell damage and death have been observed in both neural stem cells and differentiated neurons, with alcohol causing concentration- and time-dependent neurotoxicity (97). As a result, chronic alcohol consumption causes a decrease in brain volume and memory impairment (98). Research shows that alcohol exposure during pregnancy can lead to a spectrum of fetal alcoholic FASDs (Mohseni,

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Khaksari, Khoramrooz, Rafaiee, & Mirrezaie, 2023) by causing defects in neural development through mechanisms such as disruption of cell adhesion molecules, dysregulation of nitric oxide-mediated signaling (99), and inhibition of N-Methyl-D-aspartate receptors (NMDARs). In addition to the production of reactive oxygen species (ROS) and oxidative stress, alcohol consumption is a risk factor for the activation of silent sperm genes and can also have negative effects on ovum health (100). These epigenetic changes in genes may be transmitted through fertilization and cause abnormalities in the fetus.

Moreover, the use of drugs and cigarettes has become a global problem and causes many deaths worldwide every year (101). The use of drugs and stimulants causes various complications, and their negative effects on the nervous system are undeniable (102). In chronic drug use, the volume of gray matter is significantly smaller, and the density of gray matter is lower in the frontal, occipital, and temporal lobe areas, including the parahippocampal gyrus than in nonusers (103). Smoking/drugs have deleterious effects on sperm motility, viability, DNA fragmentation, sperm zinc levels, and seminal fluid ROS levels in men. They are directly related to the amount and duration of smoking (104). The exposure of laboratory animals to cigarette smoke/drugs induces oxidative stress, telomere shortening, and apoptosis in oocytes and compromises fetal development in vivo (105). It also has negative effects on the ovum and reproductive organs of women. Smoking/drugs during pregnancy endanger the health of the fetus and cause negative complications in the structure and function of the brain of the fetus (106). Therefore, smoking/drug use can cause defects in the brain of the fetus through male and female sex cells and pregnant mothers, thus challenging the next generations.

Circadian Rhythm Disruption and the Human Brain

In the present era, people have managed to control electricity and use it in various lighting devices at night. Humans who have had a regular circadian cycle (sleep and wake cycle) for hundreds of thousands of years now have a different circadian cycle. Thousands of years ago, after sunset, human activity decreased, and people slept earlier at night, but now it is not like that (107). With the advent of lighting and entertainment devices such as televisions, all kinds of computers, and smartphones that can run various programs and games, people sleep very late at night (108). However, what are the negative effects of today's circadian cycle on health? The hormone melatonin is secreted from the pineal gland of the human brain in response to darkness and during the night, and its production and duration of secretion are directly dependent on the length of the night (109). Because melatonin production is tightly linked to the light/dark cycle, the main systemic action of melatonin is to coordinate behavioral and physiological adaptations to circadian and seasonal cycles. Notably, maternal melatonin programs fetal behavior and physiology to adapt to the light/dark cycle of the environment after birth (110).

Circadian rhythm disruption can cause complications in the body (111) including problems in the central nervous system. Irregular sleep-wake rhythm can reduce learning and memory. (112). The results of studies have shown that regularity in circadian rhythms is important for fetal brain development; as a result, circadian rhythm disruption can be predicted to cause some degree of physiological and cognitive defects associated with developmental defects of the brain in these children (113). Moreover, the regularity of the circadian rhythm can affect the reproductive system of females and their sex cells (114). Compared with working day shifts, evening/night/rotational shifts reduce mature oocyte production (115), and this problem is associated with a decrease in melatonin levels during night shifts (116, 117). Although melatonin secretion in the fetus does not begin until after birth, during fetal time, maternal melatonin affects the fetal brain (118). Therefore, interfering with the mother's melatonin production during pregnancy and the lack of a normal melatonin

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rhythm can cause a decrease in neurogenesis in the fetal brain, which can hinder the normal development of the fetal brain (119). Human melatonin receptors are even expressed in spermatozoa (120). Normal levels of melatonin increase the total antioxidant capacity of semen, thereby reducing sperm DNA damage caused by oxidative stress. As a result, interference with the circadian cycle can endanger sperm health by reducing melatonin levels. Circadian disruption, which can be caused by various factors, such as working night shifts, compromises ovum health by affecting female reproductive structures.

Electromagnetic Waves and the Human Nervous System

Now, the Earth is like an electromagnetic sea. With the advent of various technologies, such as radio, television, mobile phones, internet modems, satellites, and radio and television stations, human life has become full of electromagnetic waves. These waves can have negative effects on human health (121). The results of these investigations revealed adverse effects, such as abnormal fetal growth (122) and increased DNA damage (123), in the brain cells of animals exposed to electric and magnetic radiation (124). Today, most people in the world use mobile phones, and mobile phones, as tools for entertainment and communication, and business tools, have become part of the human body, and their owners carry them with them permanently. The waves generated by mobile phones are harmful to human health (125), and the electromagnetic field and radio frequency generated by mobile phones can damage DNA. Studies have shown that long-term phone use raises the risk of brain cancer (126). The results of experimental studies have shown that exposure to electromagnetic waves, depending on the frequency and duration of radiation, can damage sperm and induce apoptosis (127). Studies have shown that the use of mobile phones by mothers during pregnancy increases the likelihood of behavioral problems in their children. It has been reported that the blood-brain barrier becomes more permeable as a result of the use of mobile phones; as a result of this increase in permeability, it can damage brain tissue (128). Reports show the blood-brain barrier becomes more permeable from using mobile phones (129). This increased permeability can damage brain tissue.

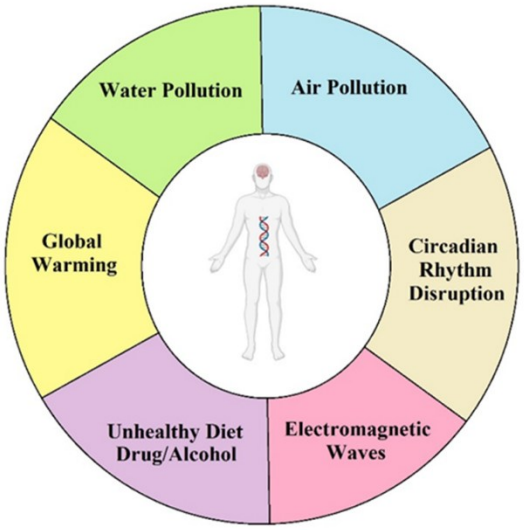


Figure 1. Schematic representation of environmental factors and new lifestyles can be great challenges for human brain function and development.

Conclusion

Almost all evolutionary scientists agree that today's intelligent man is the result of mutations induced by the environment to make him more adaptable. Although in the past, the only cause of mutation was natural environmental conditions, many more mutagenic factors have been created by humans. Humans now live in a homemade laboratory called Earth and have challenged their evolution, which has been progressing for hundreds of thousands of years on the way to creating modern human species. The artificial conditions created by humans can pose a great challenge to the human brain, which is the most evolved organ on the planet. Polluting the air, polluting the water in various ways, using a diet that includes many sugars, fast foods, and other processed foods, and the new circadian cycle have had negative effects on the human brain (Figure 1). Suppose you put a laboratory animal in a cage that is similar to the climate of today's planet

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and uses a polluted climate (contaminated with all kinds of pesticides and heavy metals) similar to the human living environment and food similar to types of fast food as well as exposure to drugs/alcohol. Along with these cases, what happens if you instill an unnatural circadian cycle similar to the modern man? The answer is clear; new conditions can have negative effects on it. Although this example may be a little strange, with a simple look at human society, many similar examples can be seen. In addition to humans, even the life cycle of animals and plants today has been affected by human activities in various ways. Pollutant weather can directly affect animals and plants, both those that humans use as food and those that are not in the human food cycle. As a result, it can be said with certainty that man has not faced such problems as much as in the present era throughout his entire evolutionary history. Today, the human brain, which has been created as the most evolved organ among all living organisms over hundreds of thousands of years by evolutionary processes, is now challenged by the destructive activities of humans. The destructive activities of humans and their new lifestyle also have negative effects on sex cells, in addition to affecting pregnant mothers and their fetuses and causing negative effects on the brains of these fetuses. As a result, children born also have defects in their brains. Therefore, the nervous system of successive generations can suffer irreparable problems.

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Authorship

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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