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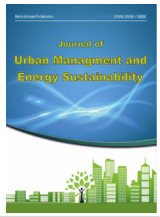

ORIGINAL RESEARCH PAPER

Explaining the Conceptual Model of the Effects of Architecture on Epigenetic Changes in Healthy Buildings: A Meta-Analysis Approach

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ABSTRACT

Access to a healthy life as a fundamental human right underscores the importance of designing healthy buildings. By integrating principles from architecture, medical sciences, and psychology, healthy buildings aim to minimize adverse effects on users' health. In a similar vein, epigenetics, which can examine environmental factors by turning generational genes on and off and affects gene expression, has shown interest in the impact of architectural spaces on epigenetic changes in individuals over time. Epigenetics aims to identify the dynamic changes in a cell's transcription potential, which may or may not be heritable. Designing a healthy building and its effect on genetic health has been a hotly-debated issue and requires more investigation. This study attempts to understand whether architecture affects genetics, how the result could be, and what architectural features influence genetics. This descriptive-analytical research employed the Delfi method and content analysis to analyze the data. The ultimate goal of this research is to compile and present the principles of healthy building design from an epigenetic perspective to leverage architecture as a tool for treating epigenetic diseases in the future. This study attempts to explain a conceptual framework for the effect of architecture on genetic and epigenetic changes by examining relevant theories and meta-analyses of existing studies of environmental architecture effects on health, genetic, and epigenetic disorders. Future studies and experiments can focus on genetic diseases caused by building architecture.

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1. Introduction

Throughout urbanization, humankind has always thought about creating a space that could provide comfort, beauty, and hygiene to increase the quality of life in their environment. That is why the concept of an ideal city has been a significant consideration for thinkers in many countries. Although the achievement of a perfect society has been less realized, humans have always aspired to move toward it. Today, health, nature, and human psychology are among the fundamental approaches to explaining the position of environmental architecture and the necessities of sustainable development. Various studies have been conducted in psychology, environmental studies, and genetics (Maartensson & Loi., 2022; Kellert & Calabrese, 2015; Wilson, 2010; Moore et al., 2003). Sustainable human development has environmental, social, economic, legal, cultural, political, and psychological aspects. According to Tylor, sustainable human development has two important principles: first, sustainable human development requires an independent understanding of local needs and resources, and second, action must result from a combination of bottom-up and top-down planning. In this regard, there is growing research on the ecology of the city and the nature of the healthy city (Milliken et al., 2023; Pedersen Zari et al., 2020; Pawlyn, 2016; Söderlund & Newman, 2015; Kellert et al., 2015; Clark & Chatto, 2014; Browning et al., 2014; Wells, 2011; Berkebile & McLennan, 2004).

According to Professor Duh. L. & Hancock, a healthy city is constantly creating and improving its social and physical environments, with the health of all citizens and a commitment to reducing traffic, addressing safety issues, pollution, and noise through various mechanisms being essential topics in a healthy city. However, building issue as part of the built environment and urban planning has been discussed less in these discussions. Buildings that cannot meet individuals' physical and functional needs endanger their users' health, and since a healthy life is the most fundamental human right, creating healthy buildings is vital. In the field of health, architectural design and its impact on genetic health is a thought-provoking issue, so questions in this regard are necessary. Does architecture affect genetics? If yes, what is the effect? What architectural features influence genetics? Epigenetics is the study of environmental factors that turn genes on or off. Epigenetic changes are essential in regulating the complex network of gene-environment interactions. Epigenetic changes resulting from environmental stress may disrupt differentiated cellular functions and produce diseased phenotypes (Kumar Mishra et al., 2021).

Maintaining a healthy life requires a balanced interplay between lifestyle factors and the epigenome. Lifestyle events, such as diet, physical activities, and environment, are crucial in shaping a healthy phenotype. These factors can modify epigenetic marks, leading to the development or prevention of non-communicable chronic diseases (NCDs), including cancer, diabetes, and cardiovascular diseases (Olalekan Sanusi et al., 2021).

In December 2019, doctors in Wuhan, China, observed unusual cases of pneumonia. As the cases increased and the virus spread globally, the World Health Organization declared the new coronavirus outbreak the sixth public health emergency worldwide (Tavakoli et al., 2019, 433). Designing a healthy building is also essential to managing infectious disease crises. Genetic characteristics contribute to health and non-infectious diseases, such as cancer and diabetes, and infectious diseases, such as Corona. The current conditions of the world and Iran highlight the implementation of many policies based on genetics and necessitate defining the role of architecture in this field. In light of these cases, this article aims to explore the impact of architecture and environmental design on genetic changes, which may take years or centuries to manifest, and develop a conceptual model on the effects of architecture on epigenetic changes for the first time.

2. Materials and Methods

2.1. Research Methodology

The nature of this research is both fundamental and cognitive. The research methodology used is descriptive-analytical, and the data was collected from library and documentary studies. In the initial stage, the descriptive-analytical method was used

to scrutinize the literature and theoretical bases, examine components optimizing the quality and function of buildings, and develop the criteria for healthy building designs from an epigenetic point of view. Following that, the Delfi method was used for the data analysis and the compilation of Tables. A pilot questionnaire was prepared to extract the primary components of the theoretical foundations of the study from quantitative data. Another data set was gathered in a qualitative form from experts and specialists to select the most effective components. The survey method (general citizenship questionnaire) was also employed in preparing reports related to the effects of architecture on physical and mental health. Also, qualitative content analysis was used to examine the experts' thoughts. The data was treated inductively, and relevant chunks were chosen and coded. Codes with comparable qualities were categorized by evaluating, rejecting, and synthesizing the data gathered during peer debriefing.

Furthermore, we used the logical reasoning method to develop the conceptual model. The theoretical studies related to the research topic were summarized. Then we analyzed the findings about architecture and environment's direct and indirect effects on health or genetic and epigenetic disorders and diseases. The design criteria for a healthy building were also analyzed from an epigenetic point of view. We also examined All available studies, sources, and research on the subject in Iran and around the world, and the model was explained using the meta-analysis method.

2.2. Literature Review

2.2.1. Healthy City

Human beings require a healthy shelter to sustain their lives. Research on creating a healthy city dates back to ancient Greece. Plato attempted to define indicators of a healthy city in the book "Republic" (Plato, 2005). With the increase in the world population after the industrial revolution in Europe, the growth of cities and urbanization led to the destruction of the natural environment and environmental pollution, which adversely affected human health. As a result, the priority of health regulations over urbanization was emphasized, first in Europe and England in 1832. An ideal healthy city was introduced in 1870 that had clean air, a public transportation network, a small neighborhood medical center, and sanatoriums for the elderly and mentally challenged where the sale of tobacco and alcohol was not permitted (Shuai, 2018:36). These ideas led to the concept of the city garden by Howard, the English city planner, in 1889 as a technical solution to tackle the problem of dirty and crowded neighborhoods (Bahrainy, 1995:14).

In 1984, at the end of the "Beyond Primary Health Services" conference in Toronto, Canada, Professor Duh. L. presented a new synthesis combining ecological and comprehensive health perspectives (Papoli-Yazdi et al., 2013). The idea of a healthy city in Iran was raised at the "First Healthy City Symposium" in Tehran in December 1991, and "The Municipality of Tehran set up Healthy City Headquarters" in Tehran in March 1992 (Tabibian, 1997:63). Several papers and books have been published on this topic using case studies. (Barton et al., 2019). Healthy buildings, as one of the essential components of healthy cities, have received the attention of scholars, including architecture.

2.2.2. Healthy Buildings

Palladio (1580) was the first to consider issues of environmental comfort. In 1860, Nightingale recognized that unsanitary environments in military camps and hospitals were responsible for deaths (Swenson, 2005:23). From 1800 to 1900, the expansion of medical awareness laid the groundwork for architectural standards that aligned with human physiology and health in the 1930s.

Banham (1922–1988) was one of the pioneers who advocated the integration of technology, human needs, and environmental concerns into architecture. In 1984, a Danish biophysicist used the term "Sick Building Syndrome" in a Swedish publication to describe problems with office buildings (Murphy, 2006:3). By 1990, the green building movement had begun, and in 1998, the first edition of the LEED certification was used for environmental building assessments. This certification is a national standard used for evaluating green buildings in the United States

and is also accepted internationally.

Baker Laporte et al. (2008) wrote the book "Healthy House," which introduced chemical pollutants in air and building materials. Lopez (2012) mentioned in his book "The Built Environment and Public Health" that architects such as Benjamin Marsh and Edward Bennett were concerned about high-rise buildings' density at an alarming rate and voiced their concerns about the deprivation of access to sunlight and ventilation. Todorovic and Tai Kim (2012) in an article, "Beyond the Science and Art of the Healthy Buildings Dynamic Control's Performance Prediction and Validation," stated that advances in energy efficiency and sustainability of healthy buildings were closely linked to the study of building facades' physical features, particularly dynamic sunlight control principles and optimal control of solar heat gain.

In the book "Building Materials, Health, and Indoor Air Quality: No Breathing Space?" Woolley (2016), presented materials to understand air quality better and prevent the release of pollutants from building materials.

In recent years, a growing focus has been on identifying factors that influence healthy building design. A study in eastern China identified 30 influential factors, with 16 key influencing factors (KIFs) identified as having an importance index above 80 (Mao et al.,2017). These KIFs can guide future efforts to create sustainable and healthy buildings.

The article " A review of air filtration technologies for sustainable and healthy building ventilation" by Liu et al. (2017) considered how urbanization increased city population density and caused severe indoor air pollution. To address this problem, Liu et al. (2017) guided future research and development of air filtration technology for sustainable and healthy building ventilation.

Clegg et al. (2020), in the article "Building Science and Radio Frequency Radiation: What Makes Smart and Healthy Buildings?" doubt the effectiveness of wireless systems, and argue that wired or cabled connections are not only faster and more reliable but also safer and more energy-efficient.

Xiang et al. (2021) in "Impacts of implementing healthy building guidelines for daily PM2.5 limits on premature deaths and economic losses in urban China: a population-based modeling study" propose that reducing indoor PM2.5 levels could offer a practical and immediate solution to save lives and curtail economic losses.

Song et al. (2021) introduced natural ventilation (NV) as a sustainable solution to improve building energy efficiency and reduce carbon emissions in their article, "Natural Ventilation in London: Towards Energy-Efficient and Healthy Buildings."

Environmental health has been acknowledged in Iran since ancient times, with Zoroaster discussing its impact on human health. Hakim Abu Ali Sina later emphasized the significance of this influence in various sections of the Book of Law (Shahcheraghi & Bandarabad, 2016). With the establishment of healthcare and the development of medicine, more attention was paid to the impact of environmental factors on health.

In his book "Geographical Pathology of Iran," Houshvar (2002) researched for several years, examining the health and climate of each region of Iran. He presented the damage caused by natural environmental elements and water pollutants, including soil and air, in two parts.

In his book, "Sick Building Syndrome and Diseases Related to Indoor Air Pollution," Assadi (2012) addressed the various symptoms associated with sick building syndrome, including nervous, excitatory, respiratory, skin, and sensory symptoms.

Azhdehfar et al. (2014) investigated the "Relation between Physical Environment of Architecture and Attention Deficit Hyperactivity Disorders Symptom in Tehran Children (6-10 years)".They found that some solutions such as incorporating natural light and providing access to outdoor by windows in the child's room, allocating sufficient space for physical activity and purposeful games, and using small plants and bushes in the building yard, could significantly reduce hyper-activity severity symptoms. In his article, "Application of Brain and Neuroscience in Improving the Quality of Architectural Space," Shahroudi (2014) emphasized the crucial role of the brain in processing environmental stimuli through the five senses, as well as intellectual, emotional, and intuitive perceptions. He also

highlighted the importance of collaboration between the brain, neuroscience, and architecture. In his book "Applied Climate" (2020), Kamyabi examined the correlation between climate and the incidence of diseases. Unlike prior research that has focused on exploring the impact of environmental architecture and healthy buildings on public health, this article employs an epigenetic approach. It presents a conceptual model to develop codified guidelines for healthy building design principles from an epigenetic perspective.

2.3. Theoretical Foundations

2.3.1. Health and illness

Throughout history, health has undergone significant changes, shifting from an individualistic perspective focused on the microbial theory of diseases in the early 20th century to a more holistic and global social model. In contemporary times, health has been widely recognized as a fundamental objective in various planning areas. In 1998, the World Health Organization (WHO) defined health as physical, mental, and social well-being (Figure 1). According to this definition, the term disease is the opposite of health. Any deviation from physical or mental well-being, whether apparent or hidden, is considered a state of disease (Hatami et al., 2019).

2.3.2. Genetics, health, and disease

Genetics can play a role in the development of certain diseases. Even in cases where a condition may not have a genetic component, a person's genetic makeup may still contribute to their susceptibility to the illness. It is important to note that individual factors such as gender, age, occupation, and social class also significantly impact overall health within a society (Hatami et al., 2019, 49). Additionally, researchers like Michel argue that quality of life is intricately linked with health (Figure 2).

2.3.3. Epigenetics and Health

Epigenetics refers to changes in gene activity that do not alter the DNA sequence. These changes are regulated by the epigenome, which includes all the chemicals that have been added to an individual's entire DNA (genome) to regulate gene expression. These chemical compounds are attached to DNA, hence the prefix "epi," which means above or on something in Greek. Epigenetic changes can pass through generations because when cells divide, epigenetic changes remain and may get affected

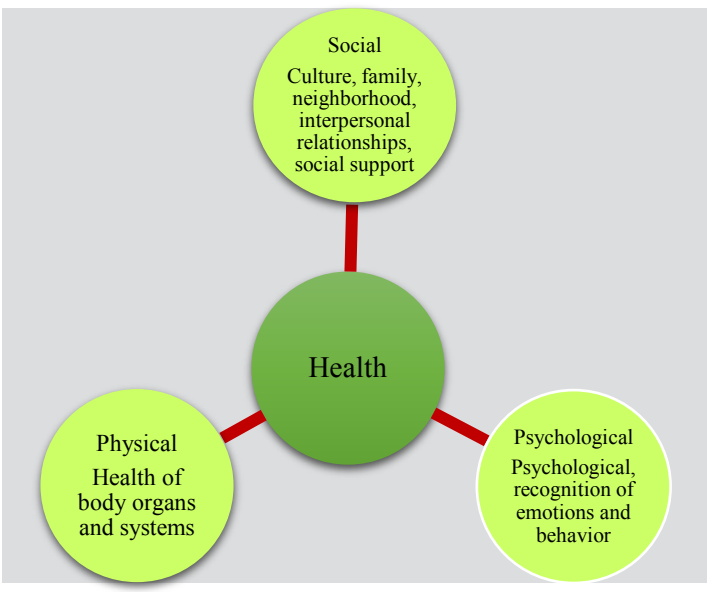

Figure 1: Individual health indicators based on the definitions of the World Health Organization (WHO)

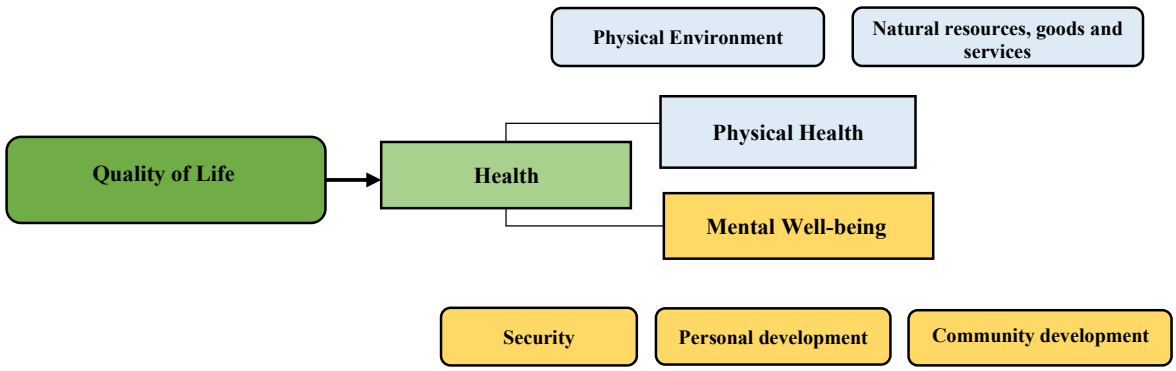

Figure 2: Components of quality of life-based on Michell's (2000) model

by environmental influences, such as exposure to pollutants and diet. The human body consists of multiple interactive systems working together to maintain overall health. The health of one system can affect the health of other systems in the body. Therefore, a person's overall health depends on the health of all interactive systems in the body (Alberts et al., 2007).

2.3.4. Health in Buildings

The importance of the environment and buildings cannot be overstated regarding human health. Unacceptable environmental conditions combined with psychological pressures can cause disruptions in health and performance in the social, psychological, and physical realms. Such conditions include noise and visual pollution, a lack of suitable housing, crowding and social conflicts, a loss of a sense of belonging to the environment, and a lack of recognition of human needs (Emamogholi, 2014).

2.3.5. Healthy Environments and Buildings

The term "human environment" today refers to the physical features created by humans and the relationships between individuals and social organizations that can affect physical and mental health. This definition, which is included in Shahcheraghi & Bandarabad's work (2016: 27), is presented in Table 1.

A healthy building does not threaten the well-being of its occupants and the environment. Therefore, healthy buildings must address two key issues: human and environmental health.

Studies show that most people spend approximately 80-90% of their time indoors, and schoolchildren spend an estimated 1,300 hours per year in classrooms (Fadey et al., 2014, 166). Healthy buildings aim to minimize the adverse effects of the environment on people's health while maximizing their benefits, which can lead to reduced absenteeism, lower healthcare costs, and improved individual and group performance. According to Emamogholi (2014), the effect of the natural and built environment on human health can be categorized into two groups:

1. Direct effects of environmental factors, air and water quality, climate, noise, and traffic, directly affect health.

2. The indirect effect comprises the designs of the built environment and their influence on people's feelings and behaviors. This includes the quality of homes, buildings (such as schools, hospitals, and workplaces), neighborhoods, the social environment, land use, access, and green spaces. It is a two-way issue: living in a poor area can negatively affect a person's mental health, and a person with psychological problems may have a negative attitude toward their living environment.

2.4. Theories of Architecture, Health, and Genetic Changes

2.4.1. The Theory of Man, Environment, and Geographic Pathology

This theory explores the relationship between

Table 1. Environment Components; Adapted from Abdul-Wahab, 2011

Aspects of environment	Definitions
Living environment	The environment encompasses the relationships between all organisms in their lives. Organisms include trees, humans, animals, and microorganisms.
Natural environment (NE)	The environment is where all living and non-living elements exist and is constantly changing.
Man-made environment / Built environment	A new and artificial part of nature, or a part of it, is created for specific purposes and to meet functional needs. This artificial environment is the habitat of organisms, such as buildings, roads, streets, parks, neighborhoods, etc.
Social Environment	A group of people living together interacts and shares a common culture.
Physical environment	An ecological or artificial boundary consists of inanimate elements, including living beings and the social environment. We call inside the skin space that separates the natural environment "internal environment," and the rest with all boundaries is called the "external environment."
Behavioral environment (BHE)	The behavioral environment emphasizes the importance of human geographic perception, mental experience, and the potential of humans as active agents in the environment."

environmental phenomena and the spread of diseases, revealing cause-and-effect relationships. Various diseases, such as lung diseases, malt fever, typhoid, malaria, inflammatory eye diseases, influenza, bronchitis, asthma, and respiratory infections, have been linked to environmental factors. In the first years of life, exposure to risks such as chemical factors, radiation, and air pollutants can increase the risk of non-communicable diseases throughout one's life (Houshvar, 2002, 76).

Research indicates that non-communicable diseases cause 2.8 million of the 12.6 million deaths triggered by environmental factors. This disproportionately impacts low- and middle-income countries, and nearly 3/4 of the deaths caused by non-communicable diseases occur in these countries. In Iran, non-communicable diseases account for over 76% of the total disease burden, highlighting the importance of addressing these issues (National Committee for Prevention and Control of Non-communicable Diseases, 2015, 32).

2.4.2. The Environmental Control Theory

Averill suggests that humans have three ways of controlling the environment:

Behavioral control: the ability to change environmental events;

Cognition control: the ability to change the way we know the environment based on that;

Decision control: the ability to choose a response to the environment.

Averill's theory also distinguishes between two types of control: primary control, in which we are comfortable with the situation, and secondary control, in which we try to adapt ourselves to the environment. In this regard, Barnes proposed the theory of personal power, and Seligman presented the idea of learned helplessness. These theories suggest that repeated failure control environmental conditions can lead to a sense of helplessness (Shahcheraghi & Bandarabad, 2016, 34).

2.4.3. The adaptation level theory suggests that individuals may unconsciously adjust to their environment, including those with high-stress levels, resulting in changes in sensitivity to environmental stimuli. This theory also introduces the concept of "environmental numbness," where individuals may become desensitized to their surroundings (Shahcheraghi & Bandarabad, 2016, 35).

2.4.4. Fritz Heider's Theory of Object and

Intermediary describes the relationship between an organism and its environment, in which the environment imposes its forces and patterns on the organism. Mediators coordinate with these forces, and people act as transmitters who obey the imposed forces of the environment and reflect them in their behavior (Francovich, 2008:44).

2.4.5. Lewin's Field Theory

Lewin's theory of the life field discusses the psychological and non-psychological forces that shape individual behavior through the psychological area of the border (spatial-temporal), which provides opportunities and obstacles that can be either motivating or hindering (Strumse, 2014:31,49; Heft et al., 2014). The functional domains of life create borderland fields where individuals and groups are actively or passively present. Non-psychological factors outside the area can affect an individual's behavior when transferred into their psychological space and studied through psychological evaluations.

2.4.6. Brofenbrenner's Theory of Human Growth: Expanding Lewin's perspective on introductory psychology, Bronfenbrenner's theory of human growth ecology criticizes individualistic views in human development and presents the psycho-social and environmental frameworks. (Bonnes & Secchiaroli, 1995,53-58), Bronfenbrenner introduces the ecological environment as interrelated structures, microsystems, mesosystems, exosystems, macro-systems, and transition systems (hierarchical levels of life events that change the individual and their surrounding environment). Each system, with unique roles, norms, and regulations, contributes to human development.

3. Findings and Discussion

This study seeks to contribute to our understanding of healthy buildings and genetic health using an epigenetic approach and proposing a conceptual model. The findings are supposed to serve as guidance for healthy building

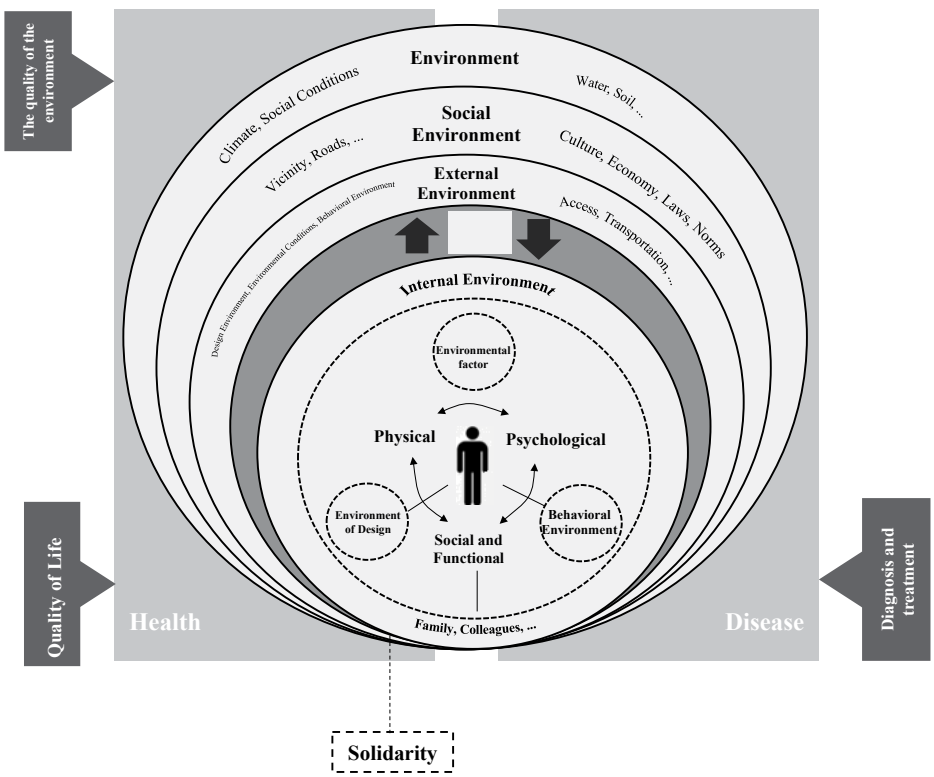

Figure 3. Environmental Variables and Consequences in Healthy Building Design

designs. Available studies show that apart from interacting with the environment, people have attempted to improve their living conditions by addressing internal deficiencies.

Based on what has been discussed, environmental factors and consequences in healthy building designs can be better captured in Figure 3.

This interdependence of humans has been the subject of commentaries by various theorists and thinkers. Today, it is well established that humans are interdependent entities inextricably linked to their surroundings rather than isolated and independent entities (MahmoudiNejad & Golabchi, 2019). Extensive research has identified the correlation between individuals' physical health and various aspects of their physical environment at work and in daily life. A variety of diseases, such as vision disorders, deafness, high blood pressure, heart diseases, digestive disorders, pain, allergies, burns, Legionnaire's disease, dizziness, memory loss, and various types of cancer, are some of the biological factors linked to the built environment and artifacts (Rate, 2000: 215).

Developing the conceptual model of healthy building design based on the epigenetic viewpoint requires knowledge of the body systems. This detail can be seen in Table 2. The Building Construction Performance Center at Carnegie Mellon has identified ten indicators to assess the significance of decisions made during the design phase for human health. These indicators include respiratory, digestive, vision, hearing, skin, skeletal-muscular health, blood circulation, the nervous system, reproductive health (including reproduction), and mental health.

The design of buildings and the environment can also affect various body systems, including the respiratory, endocrine, and nervous immune systems, as well as the muscular, skeletal, cardiovascular, and lymphatic systems.

Table 2. Body systems and their function; Adapted from Bluyssen, 2009

System	Organs	Functions
Cardiovascular System	Heart and blood vessels	Blood circulation
Digestive System	Mouth, including tongue and teeth, esophagus, stomach, digestive tubes, liver, pancreas, gall bladder, and salivary glands	Ingestion, digestion, absorption, and excretion of food
Immune System	White blood cells, thymus, lymph nodes, and lymph channels	Defense against pathogens
Integumentary System	Skin, hair, and nails	To cover and protect the body
Muscular System	Muscles attached to bones.	It consists of tissues that work with the skeletal system to control body movement.
Nervous System	Central nervous system (brain and spinal cord) and peripheral nervous system	It controls sensory processing and communication and the functioning of various systems.
Respiratory System	Nose, larynx, trachea, and lungs (six)	Inhale and exhale
Skeletal System	Including the body skeleton	Maintaining body structure
Urinary System	Kidneys, ureters, bladder, and urethra	Urine output
Reproductive System	Gonads and internal and external sexual organs	The reproductive system produces gametes in both sexes.
Lymphoideum System	Lymph nodes	Metabolism of lymph nodes in interstitial fluid
Endocrine System	The main endocrine gland and gonads are next to the organs	They transmit the signals of different states and function changes from one organ to another.

3.1. Sick Building Syndrome (SBS)

The World Health Organization has recognized the relatively recent phenomenon of building-related illness as a disease. Studies have shown that sick building syndrome and other building-related diseases can decrease worker efficiency and productivity, and improving the work environment has been shown to improve performance significantly.

Building syndrome is a relatively new phenomenon that has been recognized as a disease by the World Health Organization. According to recent studies and research, individuals living in a building suffer from unexplained symptoms of illness, which can be characterized by a sense of malaise (Kamelnia, et al., 2016). Another defining feature of SBS is that it leads to various irritating and psychological symptoms that arise within a few minutes or hours of entering the building and disappear only after being outside the building for 30 minutes to several hours. The World Health Organization has listed several complications associated with SBS, including symptoms of irritation such as a runny nose, burning and itching, throat and nasal irritation, dry skin, and a dry cough, as well as general and psychological symptoms such as headaches, dizziness, difficulty concentrating, and fatigue (Assadi, 2012).

3.2. Building-Related Illness (BRI)

This illness affects only a small percentage of individuals. However, research shows that sick building syndrome and other building-related diseases can cause a significant decrease in the productivity and efficiency of workers. Studies conducted after improvements to the work environment have shown an improvement in worker performance by over 40% (Rahbari, 2023). It is important to note that BRI and sick building syndrome are directly related to the work environment and stress.

3.3. Multiple Chemical Sensitivity Disease (MCS)

This illness affects individuals with a very high sensitivity to everyday chemicals such as paints, sprays, and perfumes. Symptoms of MCS include itchy eyes, dizziness, sore throat, and nausea. The best and healthiest way of life for those suffering from MCS is to remove any chemical smells from the indoor air (Bluyssen, 2009, 20).

3.4. Chronic Fatigue Syndrome

This illness is caused by long-term stress and nervous tension lasting at least six months. Women comprise 80% of the patients (Holmes et al., 1988, 387).

3.5. Epigenetic Disorders Caused by Architecture

Mental health refers to adapting to normal cognitive and nervous pressures in life and the work environment while remaining productive and participating in life. The psychological effects of the work and living environment can lead to stress, anxiety, depression, and isolation, which can ultimately result in psychological disorders such as pessimism and personality disorders.

a) Fatigue and disability: "Kaplan" describes "fatigue" as the disorders caused by everyday and monotonous communication that lead to irritability, sensitivity, poor manners, reduced tolerance, increased mistakes, and risk-taking. It also refers to a process in which the individual's capabilities are not responsive to the demands of the perceptual environment. According to available statistical studies, Turkey has the highest number of people with fatigue syndrome, followed by Iran. The global burden of this disease has remained almost constant (National Committee for Prevention and Control of Non-Communicable Diseases, 2015, 40).

b) Stress is caused by a lack of balance between an individual's perception of the demands of their surrounding environment and their evaluation of their ability to respond to those demands (Evans & Cohen, 2004). The symptoms of stress can vary and include physical ones such as back pain, headaches, stomach and intestinal discomfort, heart palpitations, and reduced ability. A stressed individual may feel tired but find it difficult to relax and sleep.

c) Temporal traits: Temporal traits, such as happiness and violence, are polygenic traits whose inheritance process can be attributed to epigenetic mechanisms (Malmir et al., 2016). Based on the concepts raised in behavioral epigenetics, happiness, and violence, which are considered acquired traits, can become genetic traits in successive generations by the changes the environment creates in gene expression.

Table 3. Effects of Architecture and environmental designs on Genetic and epigenetic changes

International experts and professionals	Proposal for Architectural Design and Implementation Plan	Components and parameters involved in architecture
Woolley, T. (2016); Söderlund, J., & Newman, P. (2015); Kellert, S. et al. (2015).	Improving the quality level of natural ventilation and modulating the effects of epigenetic changes in humans	Air quality and natural ventilation of the building
Swenson, K. (2005); Francovich, C. (2008); Fadey. M. O. et al., (2014); Browning, W.D. et al., (2014); Abdul-Wahab, S. A. (2011).	Promoting the use of environmentally sound materials and, at the same time, eco-friendly based on the climate and geographical environment of each region	Chemical building materials and reducing physical health
Wells, M. (2011); Moore, K. D. et al. (2003); Abdul-Wahab, S. A. (2011).	Considering the human thermal comfort zone in the design of the environment and the inhibitors of changes in thermal parameters	Heat and cold and thermal comfort in the architectural environment
Mao, P., et al. (2017); Fadey, M. O. et al., (2014); Baker-Laporte. et al., (2008); Abdul-Wahab, S. A. (2011).	Having architectural strategies to adjust (decrease or increase) the humidity of the artificial environment	Ambient humidity
Olalekan Sanusi, K. et al., (2021); Xiang, J. et al., (2021); Fadey, M. O., (2014); Berkebile, B., & McLennan, J. (2004); Baker-Laporte, P., Elliott, E., et al. (2008); Abdul-Wahab, S. A. (2011).	Reducing environmental pollutants and environmental suspended particles through architecture and its practical solutions	Dust and air pollutants
Kellert, S. et al., (2015); Kaplan, S., (1995); Song, J. et al., (2021).	Having maximum natural light and direct connection with the natural environment in architectural design	Quality of light and brightness
MahmoudiNejad & Golabchi, (2019); Kellert, S. et al., (2015); Clark, E., & Chatto, CH.F., (2014); Heft et al., (2014); Abdul-Wahab, S. A. (2011).	Paying attention to the psychological effects of colors in interior design, especially for special groups such as autism etc.	Color design in architecture
Wilson, E.O. (2010); Lopez, R. P. (2012); Xiang, J. et al. (2021); Francovich, C. (2008); Clark, E., & Chatto, CH.F., (2014),	Reducing the amount of stress caused by architectural design and ways to improve human-environmental vitality	Stress and mental functions
Strumse, E. (2014); Francovich, C. (2008). Clark, E., & Chatto, CH.F., (2014); Berkebile, B., & McLennan, J. (2004).	Paying attention to the design dimensions of reducing depression and inducing vitality in the design	Depression and serotonin inhibitors
Murphy, M. (2006); Moore et al. (2003); Browning, W.D. et al. (2014).	Reducing environmental noise pollutants disturbing the psychological comfort zone in environmental design and architecture	Noise and sound pollution
Lopez, W. (2012); Clegg, F. M. et al. (2020); Abdul-Wahab, S. A. (2011).	Using permaculture and urban agriculture in landscape design and architecture and improving the natural quality of drinking water in biological purification in areas with poor sanitation	Access to water and water quality
Todorovic, M. S. et al. (2012); Goldstein, W. E. (2010); Fadey, M. O. et al. (2014); Abdul-Wahab, S. A. (2011).	Having sports spaces in the common areas of residential buildings or at least accessible to users	Sports and entertainment spaces
Xiang, J. et al. (2021); Clark, E., & Chatto, CH.F. (2014).	Considering the non-use of unconventional forms with the physiological and psychological characteristics of generations	Form and shape of the building

d) Allergic and autoimmune diseases: Illnesses such as asthma and multiple sclerosis are caused by an inappropriate immune response to foreign allergens (Esmaeilzadeh et al., 2021). Recent studies have focused on epigenetic mechanisms to investigate changes in the course of diseases. The reason is the environment influences such tools. Epigenetic modifications can be affected by various environmental factors or can affect the genome. They can protect against allergies and contribute to autoimmune processes.

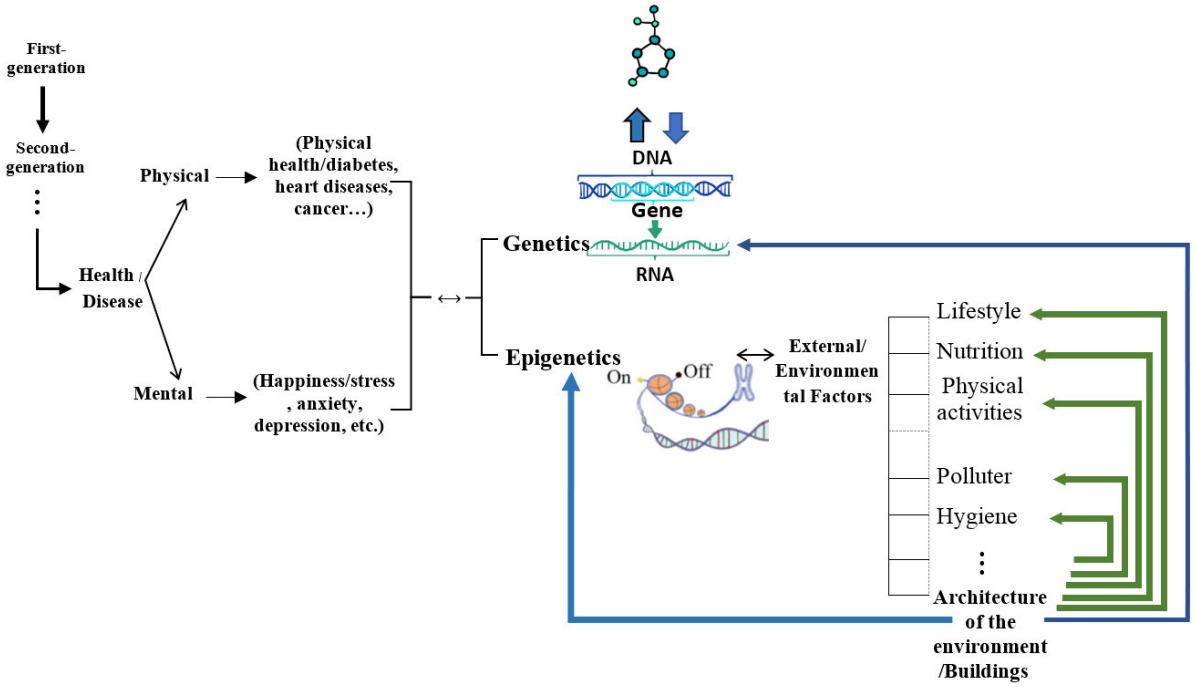

Figure 4. The influence of environment/building architecture on genetics and epigenetics (direct and indirect)

The findings related to the effects of architectural design components on genetic and epigenetic changes are presented in Table 3.

4. Conclusion

Based on the analysis of available studies, it can be concluded that health and illness have various dimensions and architecture directly or indirectly affect physical, mental, and social health/diseases and can cause genetic and epigenetic changes over time (Fig. 4).

– Examining the correlation between architectural design elements, epigenetics, and depression levels reveals the intricate interplay between environment and genetics in regulating individuals' moods, including depression, anxiety, happiness, and stress.

– Diseases caused by changes in gene expression patterns through mutations in DNA, genetic material, and gene sequences can be directly or indirectly linked to architecture.

– Similarly, alterations in the expression patterns of genes without any change in DNA sequence can modify gene function, resembling a genetic mutation. Such heritable epigenetic (paragenetic) changes are reversible and shaped by the environmental effects of architecture.

– Today, architects and psychologists concur that the architecture of a house affects people's moods and behaviors. Architecture plays a crucial role in both a culture's creation and birth. The design and management of space can manage behavior within that space.

– A healthy lifestyle requires a harmonious interaction between lifestyle factors and the epigenome. Researchers suggest that the environment and lifestyle affect genetic changes and the occurrence of genetic diseases, such as autism. Moreover, environmental factors such as diet, physical activity, and surroundings influence the development of a healthy phenotype by modulating epigenetic marks, contributing to or reducing non-communicable chronic diseases (NCDs) such as cancer, diabetes, cardiovascular diseases, and obesity.

Overall, the environment significantly impacts human development and the next generation. In general, the environment can affect the genome in two main ways.

1) It can affect the structure of the genome,

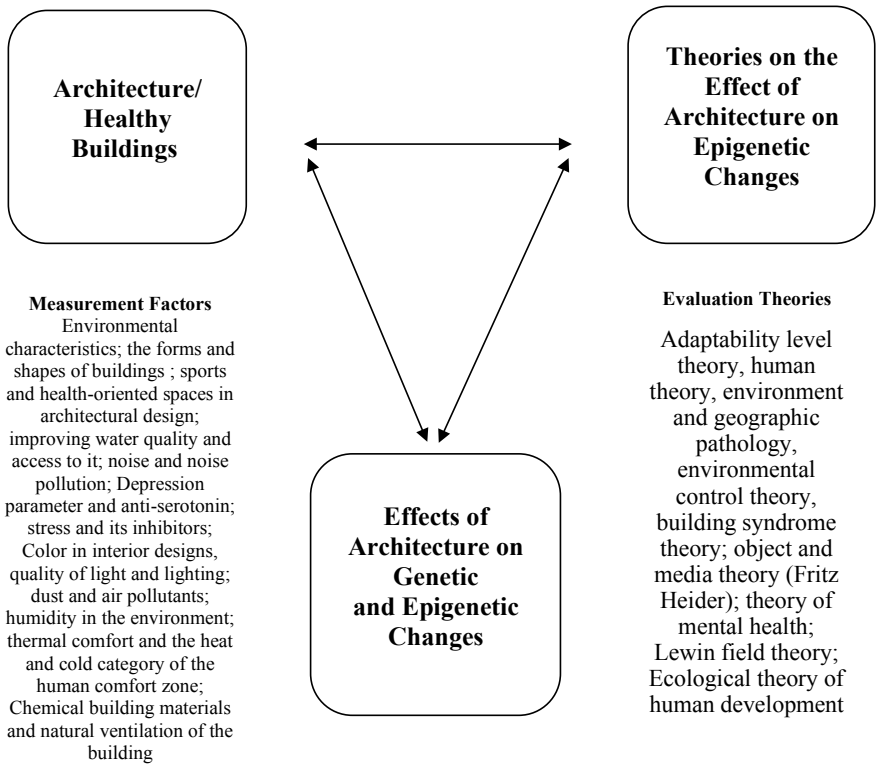

Figure 5. Explaining the model and conceptual framework of architectural effects on epigenetic changes in healthy building design

2) It can influence gene expression.

Environmental factors can cause changes in gene expression that persist in cell memory for an extended period. These changes fall under the epigenetic modifications, which can contribute to the developing certain diseases (refer to Fig. 5).

Future studies

The link between architecture and genetics is complex, and the study's findings may shed light on the emerging aspect of epigenetics, which reflects healthy architecture. The following recommendations can be made for future studies:

– By redefining architecture's unique role in genetics, and epigenetics, some researchers can take a fundamental step toward solving genetic health problems of specific genetic and epigenetic diseases.

– Some experimental studies can be conducted in laboratories to understand the causal relationship between architecture and genetics.

– Some intervention programs can investigate the effect of intelligent and healthy cities on genetic disease recovery or such effects on infertility treatment.

Conflict of Interest

"The authors declare that there are no conflicts of interest regarding the publication of this manuscript".

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