



Epigenetic and Anesthesia: Challenges and Opportunities

Fatemeh Roodneshin^{1,*}

¹Department of Anesthesiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

*Corresponding author: Department of Anesthesiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: fatemehroodneshin2020@gmail.com

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Dear Editor,

Epigenetics in anesthesia is an emerging field in medicine, and many anesthesiologists, assistants, and other doctors have little information about the relationship between these two sciences.

In epigenetics, several regulatory mechanisms, including phosphorylation, sumoylation, methylation, acetylation, and ubiquitinylation, are involved in biological processes by affecting the histone code. The relationship between anesthesia and epigenetics has facilitated the understanding of some scientific concepts. Examples of processes that have been investigated by understanding the relationship between epigenetics and anesthesia include the carcinogenic effect of anesthetic drugs, the relationship between histone acetylation and pain, the relationship between methylation of histones and memory, the role of ketamine in learning and depression, the effectiveness of glutamate and cellular skeleton, and the relationship between epigenetic alleles and malignant hyperthermia. In addition, the effect of general anesthesia on the reprogramming of the infant's brain, the relationship between epigenetic genes and neuropathic pain, and the cardioprotective role of isoflurane gas and MicroRNA-21 are also investigated in the field of epigenetics and anesthesia (1).

With the progress of science in recent years, we know that a specific sequence of DNA can express a functional protein. The data obtained from the Human Genome Project has provided researchers with valuable information on the mechanisms involved in gene regulation. These findings demonstrate that what we know as DNA coding genes constitutes only 1.5% of DNA. Investigating the function of other parts of DNA is the responsibility of the National Genome Research Institute in the United States. During this research project known

as ENCODE, scientists discovered that 80% of human genetic material is related to at least one biochemical process, the process of regulating the expression of coding genes (2-4). For this reason, many types of RNA are not translated into protein, and gene regulation is a very complex process. Non-coding RNAs include many small nuclear RNAs, tRNAs, ribosomal RNAs, or some long RNAs. The expression of proteins is carried out by the cooperation of miRs and a large number of target mRNAs. miRs are strings with a length of 19 to 22 nucleotides combined with their complementary sequences in the mRNA string and play their role. It is demonstrated that if miR binds to a specific gene, it causes gene destruction or silencing. Mature miR has 5 to 7 nucleotides and can bind to mRNA. The interactions between mRNA and miR create a complex network of post-transcriptional regulatory factors. One study investigated miR-21 role in cardiac protection against ischemia-reperfusion complications. The researchers did not use the ischemia-reperfusion model in the wild and miR-21 knock-out mice. Based on their results, miR-21 is a factor that can reduce the damage caused by ischemia-reperfusion by means of activating cardiac protective molecules. The expression of miR-21, observed in structures such as smooth muscle cells, vascular endothelial cells, and cardiac fibroblasts, can increase or decrease under the influence of chemical inhibitory agents (3). Therefore, the design of treatment strategies based on regulating cardiac genes has a promising future in medicine.

Watson and Crick demonstrated the structure and function of DNA for the first time in 1957. A few years later, Waddington explained the process of cellular adjustments using images and a multidimensional epigenetic model (1). Waddington's findings showed that the diversity of humans is not limited to the one-to-one expression of

genes and the production of proteins and asserted that a set of complex internal and environmental interactions are influential in this regard. For many years, many researchers have been interested in understanding these complex interactions. Recent findings indicate that miRs and protein expression in their cell of origin can also be present outside cells and in the circulation and are secreted in exomes. These miRs are derived from external sources such as viruses and plants (5).

Our new knowledge in the field of epigenetics allows anesthesiologists, residents, and other physicians and researchers to understand the role of general anesthesia on functions such as learning and memory, the effect of ketamine on depression and pain perception, the role of surgical stress on the brain, and the performance of local anesthesia (6).

Epigenetics can also facilitate the interaction of anesthetic-induced carcinogenic drugs, prevent hyperthermic malignancy, and control and manage chronic pain. Understanding the epigenetic mechanisms and finding the relationship between external and internal factors can predict current events or future injuries. Many behaviors and emotions we experience daily, such as depression, various tumors, the ability to learn skills, memory, or even personal behaviors, are related to epigenetic factors. Researchers believe methyltransferase inhibitors can be used instead of general anesthesia, and local anesthetics can be used in some surgeries with minimal side effects. It seems that in the future, with the demonstration of successful cases of epigenetic anesthesia and the minimization of its side effects, it would be possible to pinpoint the most appropriate anesthesia method for each patient in treatment plans (7).

Investigating the relationship between anesthesia and epigenetics is an interesting and novel research topic. Although the sparsity of studies conducted in this field makes it difficult to search for the background information, today, details of the link between epigenetics and anesthesia have been demonstrated, which can pave the way for future research. For example, investigating the relationship between stress and pain, DNA methylation and protein transcription and its role in inflammation, and the effects of inhaled anesthetics on cognitive functions are among the evidence that clearly demonstrates the relationship between epigenetics and anesthesia. Therefore, it is imperative to develop programs and protocols based on which nurses, anesthesiologists, students, and researchers can learn the most appropriate and latest methods of using anesthesia and epigenetics to improve patients' health.

Footnotes

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