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Gene-Environment Interaction

"Early life experiences could leave epigenetic marks and alter the expression of several neuronal genes in the brain resulting in remarkable changes in behavior later in life"

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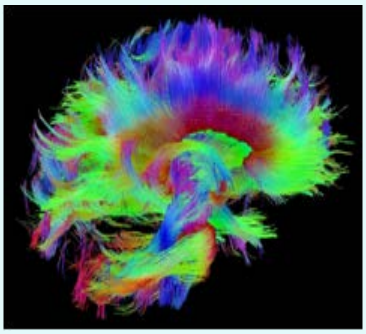
COLUMN ARTICLE

Scientists have long debatedwhat shapes various aspects of human behavior-nature or nurture, genes or the environment. They are both important and interdependent. They cannot be teased apart during the course of human development. Genes are an important part of who we are, but ourearly life experiences, lifestyle choices, diet, exposure to toxins or stress could affect the way these genes are expressed and how they function. It has been shown that environmental factors could spatially and temporally activate a network of "chemical switches" within our cells known as the "epigenome". Within a specific context, this epigenome interacts with our genome and affects when and how much of our genes will be expressed as well as their level of activity. This is what we know as gene-environment interaction, or "epigenetics".

Historically, the term "epigenetics" was first defined by the British developmental biologist Conrad Waddington as "the branch of biology which studies the causal interactions between genes and their products, which bring the phenotype into being" (Waddington, 1942). It is now more precisely described as a type of molecular and cellular "memory" that results in heritable stable changes in gene expression and function which are unrelated to changes in DNA sequence. Epigenetic mechanisms are quite complex and include postranslational modifications of histone proteins that package the chromatin, DNA methylation or small noncoding RNAs. It is becoming clear that these mechanisms interact to influence gene expression and activity. Epigenetic dysregulation of gene expression has been linked to many diseases, including neurological diseases or disorders. Studies have revealed that epigenetic changes could have long-term effectslater on in life if theyoccur during early development and could be transgenerational. Could we override the effects of these earlier influences for a better outcome? There is a potential for reversibility if environmental factors are favorable.



www.humanconnectomeproject.org

Our brain is plastic. It is capable of change and is responsive to our environment. Let's take care of it!

Several studies have revealed that early life experiences such as maternal care, trauma, severe stress, diet, toxins, or drug abuse could leave epigenetic marks and alter the expression of several neuronal genes in the brain re-

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sulting in remarkable changes in behavior later in life.The elegant work of Meany & Szyf at McGill University showed that the quality of maternal care during early life in pups altered their stress reactivity later on during adulthood. Jirtle & Skinner were pioneers who showed that exposure to environmental factors during early development, such as maternal diet or maternal exposure to toxins, increases offspring vulnerability to diseases later on in life. They also showed that these changes could be transmitted to the subsequent generations. Studying gene-environment interactionsin humans isvery complicated. We rely on animal models and functional analysis of large data sets that are most often derived from genomic, proteomic and bioinformatics tools, which demonstrates the limitations of this multidisciplinaryresearch. Another example of a strong and common environmental factor is alcohol. Studies have shown that alcohol addiction, a complex brain disease, is also induced by genetic and epigenetic factors.

Alcohol is one of the most popular and most abused drugs in our society. About 150 years ago, some people in England started to speculate that alcohol was harmful. William Hogarth depicted in his famous painting "London Gin Epidemic" the horrors that happened in the 18th century and the adverse consequences of drinking during pregnancy.Lemoine., *et al*. (1968) published the first article which established a connection between maternal alcohol consumption during pregnancy and abnormal fetal development. Jones., *et al*. (1973) systematically delineated the association between maternal alcohol abuse and specific birth defects and provided diagnostic criteria for this condition, now known as Fetal Alcohol Spectrum Disorder (FASD). Recently, Govorko., *et al*. (2012) showed that exposure to alcohol during fetal life causes epigenetic changes in the rat's hypothalamus resulting in an increased stress reactivity during adulthood. More importantly, these fetal alcohol-induced effects were also seen in multiple generations.

Adolescence is another critical developmental period where the brain is extremely malleable and undergoes substantial rewiring in response to environmental factors (McEwen, 2008). In 2012, the National Institute of Alcohol Abuse and Alcoholism estimated that 17 million people in the US have alcohol use disorders(AUDs) that could reach the level of addiction. In particular, binge-drinking during adolescence is on the rise, which will have long-term negative health consequences including increased susceptibility to seizures and stress-related disorders later in life. Injuries to the young brain can result in increasingly serious, prolonged, and expensive consequences to the older brain.

The completion of the Human Genome Project (HGP) in 2003 allowed us to precisely sequence and map all the genes in the human genome.The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, launched in 2013, will provide us in the near future with a dynamic picture of the brain that we have never seen before, revealing how its circuitry is altered in response to a wide range of environmental factors. Understanding how a normal brain functions in comparison to a diseased brain will identify novel avenues to understand the complexity of human behavior and to help people live longer and healthier lives.