Psychology Today

Sylvia R. Karasu M.D.
The Gravity of Weight

Double-crossing the Double Helix: Weight & Genes,

Metabolic imprinting and drifting through the "epigenetic landscape"

Posted Aug 05, 2012

Epigenetics involves modifications of genes without modifying the gene's structure

Source: istock.com/Inok/used with permission

Most researchers believe that there is considerable genetic input in determining who will become obese--perhaps up to 70% or so in some studies, if you are unlucky enough to have two obese parents. Scientists, though, from an evolutionary perspective, do not believe that our genes have changed significantly in such an infinitesimally short period of time. So why has the prevalence of overweight and obesity become epidemic or even globally pandemic in the past thirty years? That is where the science of epigenetics enters our picture.

Epigenetics and the concept of the *epigenetic landscape* are terms that were first used by C.H. Waddington in the early 1940s (well before the field of molecular biology) to describe all the biological processes that can occur during development that interact with genes and result in how an organism actually appears (i.e., its phenotype.) Choudhuri, in an 2011 article on the history of epigenetics in the journal *Toxicology Mechanisms and Methods*, explains that originally, epigenetic mechanisms were almost seen as “metaphysical and without any understanding of their molecular underpinnings” and became a “default explanation” when genetics failed to explain a particular phenotype.

More recently, *epigenetics* is defined as any long-term, persistent change in gene function that does not actually involve any alterations in a gene sequence or structure. Essentially, though, epigenetics, while *not changing a gene's sequence or structure,* does involve modifications to a gene that can be inherited from one cell to another or even from one generation to another. These modifications, for example, may lead to either silencing or activating genes and may be adaptive or nonadaptive. We now know they may *include* adding or subtracting methyl groups (a carbon atom bonded to three hydrogen atoms) called "methylation," changing the configurations of histones, (proteins around which the genetic material DNA winds in a cell's nucleus) or even producing small (called micro) strands of RNA. (RNA is the nucleic acid involved in protein synthesis and many biological reactions including controlling genes but unlike the double-stranded double-helix configuration of DNA, it is single-stranded and has different chemical components.) Epigenetic modifications can be reversible or stable, as well as occur randomly ("stochastically") or induced by changes in the environment.

Choudhuri describes epigenetic mechanisms as "an editorial hand that edits and modifies the language of DNA," but adds that we still don't understand what "regulates the regulator," i.e., "how signals trigger epigenetic changes."

We are the product of our DNA and the environment, both in utero and outside

So even though we have been successful in mapping the human genome, we have been less successful in assessing the contribution of any exposures in the body's internal as well as external environment, whenever those exposures appear. The *exposome* (a term first used by Christopher Wild) is the "totality of exposures" received from conception throughout life. Howard Slomko and his colleagues at Albert Einstein College of Medicine, in a recent "minireview" of epigenetics for the journal *Endocrinology*, note that although a person's genome is fixed at conception, his or her internal chemical environment is constantly changing because of changes in both a person's internal and external environments. Exposure to chemicals, smoke, drugs, radiation, diet, and even inflammation, stress, infection, etc. may all have an impact on our DNA. Today, epigenetic mechanisms have wide-ranging implications for research in aging, cancer, and obesity.

Source: istock.com/Henrik5000, used with permission

This epigenetic landscape, from prenatal and early postnatal development and throughout childhood and adulthood, can have a signficant and sustained impact throughout life. In fact, pathologist George Martin has noted that exposure to different environments over time has been postulated to result in *epigenetic discordance* or rather poetically, *epigenetic drift*, even between monozygotic (identical) twins, who share all their genes, as they age, and may explain, for example, why one twin develops Alzheimer's Disease in his 60s and the other not until his 80s.

We are all familiar with the importance of a nontoxic uterine environment for the development of a growing fetus. The teratogen, Thalidomide, for example, taken years ago by unsuspecting pregnant women, resulted in major congenital malformations for the fetus. Less dramatic, but perhaps no less ultimately significant effects, though, may result from a pregnant woman's diet and may be responsible, at least in part, for an increased susceptibility to obesity and differences in regulation of fat and glucose in her offspring much later in life. A metabolic "obesogenic environment" *in utero*, for example, may expose the fetus to increased levels of glucose, as well as to increased levels of the hormones insulin and leptin. This has been called *metabolic priming* or *metabolic imprinting* such that nutritional exposure prenatally results in a kind of *endocrinological memory* with potentially far-reaching consequences. A gene-environmental interaction occurs: Not only you are what you eat, but you may be what your mother has once eaten!

Exposing the fetus to certain foods may predispose to obesity later in life!

Source: istock.com/Spanishalex/used with permission

About the Author

Sylvia R. Karasu, M.D., is a clinical professor of psychiatry at Weill Cornell Medical College and the senior author of *The Gravity of Weight.*

In Print: *The Gravity of Weight: A Clinical Guide to Weight Loss and Maintenance*

Online: my own website