

## **Stress, Genetics, and Epigenetics and Human Evolution and Development**

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Nowadays, we frequently associate the fields of Evolution, aka Genetics, and Phylogeny, and Development, aka Epigenetics, and Ontogeny, and use the abbreviated term Evo-Devo to refer to both fields. The human organism and the societies it forms are complex systems that, given the enormous impact of human cognitive and emotional empathy, should be considered together. As such systems, humans and their societies are in a relatively stable disequilibrium or homeostasis, that is maintained by extrinsic energy. Complex systems respond adaptively to exogenous or endogenous threats, the stressors, and the state of disturbed homeostasis, or stress, represents a condition that has the power to shape the ability of a species or individual to survive and reproduce. Hence, both evolution and development are influenced by stress. Major evolutionary and developmental stressors include starvation, dehydration or hemorrhage, injurious agents, presence of adversaries and tissue injury. We have adapted our physiology and behavior, both as a species and as individuals, to respond to these stressors as successfully as possible. Now, we have the benefit of the stupendous progress in biology and genetics to understand the mechanisms through which our species has evolved by adapting to and surviving through major evolutionary and developmental stressors. These selective pressures explain, to a great extent, the appearance of the modern chronic diseases of humanity, such as obesity, the metabolic syndrome, hypertension, allergies, autoimmune disorders, anxiety, depression, the pain and fatigue syndromes and sociopathic behaviors. The term Epigenesis was first employed by Aristotle to suggest the process of de novo changes in organismal responses to environmental conditions, as opposed to the inner preformation theory of Plato, who had proposed that all developmental processes were predetermined and unfolded over time. The modern definition of Epigenetics was proposed by C. H. Waddington in 1942, as “the causal interactions between genes and their products to bring the phenotype into being”. Even though epigenetics represent acquired properties that are obtained by the organism over its lifetime, i.e., during ontogeny, some may cross generations or even lead to genetically inheritable changes. The epigenetic process is effected by covalent bonds on the DNA without changes in the base sequence of the molecule, post-translational modification of proteins, DNA-binding proteins or protein complexes, miRNAs, piRNAs and other noncoding RNAs, as well as by formation of super-enhancers, which appear to play major organizational roles in tissue differentiation. Methylation vs. demethylation, as well as acetylation vs. deacetylation, of DNA and chromatin proteins represent key molecular changes in epigenesis. Epigenetic functions include embryonic cell differentiation, genomic imprinting, X-chromosome inactivation, retrotransposon repression, somatic cell differentiation, immune function, puberty, sexual orientation, right/left handedness, labor and delivery, maternal and perinatal stress, brain plasticity, memory formation and stress-related behaviors. Behavioral disorders, such as depression and schizophrenia, have a strong epigenetic component. We should note that epigenetic control mechanisms evolve, there is a Lamarckian dimension in evolution, and imprints and methylation marks are erased and reestablished de novo stochastically twice, at the gamete and blastocyst stage, in each generation.