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Life experiences put their stamp on the next generation: New insights from epigenetics

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The 18th century natural philosopher Jean-Baptiste Lamarck proposed that the necks of giraffes lengthened as a consequence of the cumulative effort, across generations, to reach leaves just out of their grasp. This view of evolution was largely abandoned with the advent of modern genetic theories to explain the transmission of most important traits and many medical illnesses across generations.

However, there has long been the impression that major life events, like psychological traumas, not only have effects on individuals who directly experience these events, but also have effects on their children. For example, cross-generational effects have been well-documented in the children of Nazi death camp survivors. Similar issues have been reported in the context of mood disorders and addiction. Until recently, these trans-generational effects were attributed to changes in the way that parents treated their children or the child's reaction to learning about the parent's history.

In the most recent issue of Biological Psychiatry, Swiss researchers from the University of Zurich and Swiss Federal Institute of Technology, led by Dr. Isabelle Mansuy, discuss how the emergence of the field of epigenetics has introduced a new component to this discussion – the trans-generational transmission of changes in the regulation of gene expression.

"The question of the inheritance of acquired traits has puzzled biologists and clinicians for decades. Although it has been consistently observed as

early as in the 18th century, the time has now come that sufficiently strong and convincing evidence has accumulated to firmly accept it," said Mansuy.

The genetic transmission of traits reflects alterations in genetic structure, i.e., the base pairs that form DNA. Epigenetics, on the other hand, involves cellular processes that do not alter the structure of DNA. Instead, epigenetic mechanisms, including the methylation of DNA or of specific residues on histone "supporter" proteins, influence the extent to which individual genes are converted into messenger RNA. These changes can occur in any cell of the body, but when they occur in the germ cells (sperm or eggs) the changes may be passed to the next generation.

The changes in DNA structure are random events that acquire functional significance in the context of Darwin's "natural selection" process. In contrast, the epigenetic reactions to specific environments are designed to enable that organism to cope with that context. When these traits are passed to the next generation, it is as if the newborn arrives prepared for that specific environment. Problems arise when the epigenetic processes give rise to traits that are not adaptive for the offspring, such as heightened stress reactivity, or when the environment has changed.

"This is a remarkable story with far-reaching implications," commented Dr. John Krystal, Editor of *Biological Psychiatry*. "There is a suspicion that epigenetic processes may be reversed more easily than genetic traits, exemplified by the development of HDAC inhibitors. This is a rapidly evolving research area that has captured a great deal of attention."

More information: *Biological Psychiatry* doi: 10.1016/j.biopsych.2012.08.019