Epigenetic Inheritance of Traits: The Impact of stress on the offspring.

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Abstract

Many people notice similarities in anxiety, fears, or weight gain between parents and children, which raises the question of whether stress leaves biological traces on DNA rather than only being learned. This review asks how external stress affects the epigenome, the collection of epigenetic marks that alter gene activity without changing the DNA sequence, and whether these effects can pass to later generations. Evidence is mixed, and some scientists doubt that such marks can be inherited at all. We critically examined three key studies: historical records linking food availability to health across generations, a cohort of people exposed to famine before birth, and a mouse fear-conditioning experiment, assessing the methodology, strengths, and limitations of each. The historical records showed sex-specific links between grandparental food availability and grandchildren's mortality, but were purely statistical and had small subsamples. The famine cohort found that starvation around conception was associated with reduced IGF2 methylation in adults six decades later, but its small sample limits generalizability. In mice, fear of an odor conditioned in fathers appeared in later generations, but the relevance to humans remains debated. Overall, the evidence suggests that external stress leaves measurable epigenetic marks and that some may be heritable, yet no clear molecular link connects animal models to human data. Future work should test these findings directly in humans with larger samples and molecular analysis.

Keywords: epigenetics, epigenome, stress, DNA methylation, transgenerational inheritance

Introduction

There is a commonly known fact that we all inherit our traits from our parents, whether this trait is minor that doesn’t affect the way our body functions, such as eye color, hair type, type of figure and etc. or the ones that affect our health such as allergies, deficiencies and so on. But at the same time some individuals notice some similarities between a child and a parent that are not related to the health and appearance at all, such as things like the ability of gaining weight, the level of anxiety or even fears, these traits are the response to the external stress that are gained throughout the whole life, but do they actually have an impact on your DNA? There is a thought that these traits cannot be physically inherited, but rather taught to children, however your DNA can be altered throughout your whole life without changing the structure itself. This question is explored in Genetics called Epigenetics. The term “epigenetics” traces to Conrad H. Waddington, who coined it in the 1940s to describe the developmental processes linking genotype to phenotype. In other terms, epigenetics is the field in genetics that studies the

"outside" of genome (complete set of genetic material or DNA (deoxyribonucleic acid) present in an organism.), epigenome which is a collection of all epigenetics "marks" on the DNA. This key term is the field that could help us answer the question: "Can the external stress be transferred to future generations?"

For this review, there is a contrast in different views from diverse perspectives. For instance, some scientists, such as Jerry Coyne, state that epigenetic marks do alter the genome, however they (scientists) doubt that these "marks" could be transmitted through inheritance. However, some other experiments made by different scientists have "proven" the fact that epigenetic marks can be transferred, but even these experiments have some flaws that make the study less reliable and accurate. In this article we will discuss these studies, talk about their significance to answering the question that was mentioned below.

Human-based Studies

In 2006 the scientists (Pembrey, Bygren et al.) tried to study the transgenerational effect by using Överkalix records from 19th century, where researchers (Pembrey, Bygren et al.)found sex-specific, line-specific transgenerational effects: a paternal grandfather's food availability during his "slow growth period" (ages ~9–12) affected grandsons' mortality only; a paternal grandmother's exposure affected granddaughters only. In ALSPAC, fathers who started smoking very early (before age 11) had sons (not daughters) with higher BMI. The authors (Pembrey, Bygren et al. 2006) proposed a hypothesis involving sex chromosomes (X/Y) as a transmission mechanism — one of the first pieces of evidence for sex-specific transgenerational inheritance in humans, though based on statistical association rather than a proven molecular mechanism. The visible strength of the methodology that scientists (Pembrey et al., 2006) used is unique historical records from Överkalix — parish registers, grain price/harvest data — allowing objective (not self-reported) reconstruction of food availability. Also longitudinal data spanned several generations of the same population created a rare opportunity for transgenerational analysis in humans. The Överkalix study (Pembrey et al., 2006) suggests that the changes in genes are transmitted from one parent to the child of the same gender, proving it by Swedish Överkalix records where the smoking habit of father from young age had sons with higher BMI, However, the one limitation that leaves the study unreliable is the small amount of subsamples that lead to very weak statistics. Also the strong evidence of unreliability of the work is that this study is only theoretical where no molecular data has been provided. Because of such strong evidence, there is a significant gap that makes it hard to use this study as a reference.

The second most significant reference for the answer to the question is a study of Dutch "Hunger Winter" (1944-45) that was carried out by Heijmans et al. in 2008. The study had shown that after 60 years the individuals whose mothers had been starved specifically during the periconceptional period (the first weeks after conception) had significantly lower methylation levels at the IGF2 (insulin-like growth factor 2) gene than their same-sex siblings who hadn't

experienced this in utero. This was direct molecular evidence that environmental exposure early in pregnancy leaves a measurable epigenetic “mark” persisting into adulthood. Like the Överkalix study (Pembrey, Bygren et al.), the Heijmans’ “Hunger study” also has a strong methodology that is studied on a human model to identify the most accurate evidence of their studies. The advantages of methodology is that during the study, scientists used within-family controls — comparisons were made against unexposed same-sex siblings of the same person, elegantly controlling for genetic background and most socioeconomic/environmental factors. But the study’s main limitation is that there was a small sample of epigenetic studies (about 60), which means that these studies cannot be accurate enough to apply on the majority of people. In addition, despite sibling controls, reverse causation (differences in methylation being a consequence rather than a cause of phenotypic differences) can’t be fully excluded, and a causal link to specific diseases (metabolic syndrome) isn’t directly proven in this work (Heijmans et al., 2008).

Animal-based studies

The other types of studies were made not on human models, but on animal modules. There are many controversies about animal models since not many correlations between animals and humans were scientifically proven to be not even similar. But, still these studies may have a significant impact on the answer to the question. The study made by Dias & Ressler (2014) was made to prove that reaction to a certain stress can be inherited as well. In the study the male mice underwent fear conditioning to the odor acetone pairing with electric shock. The results from the Dias & Resler’s study in 2014 stated that the further generation of mice had also experienced the fear reaction as they avoided the flowers that contained the odor acetone Dias & Ressler, 2014). The major limitation of the study is that it was carried on the mouse module, the correlation between mice and humans are not proven and debatable even now. This study provides what Överkalix lacked — a direct molecular mechanism (alteration of a specific olfactory receptor via the germline) and a controlled experimental design excluding behavioral/environmental transmission routes, however it still has to be carried out multiple times to achieve the more accurate results and has to prove the correlation between mice and humans (Pembrey et al., 2006).

Conclusion

In conclusion, the studies discussed in this paper provide compelling foundational evidence that external stress can be transferred to future generations through epigenetic mechanisms. Human epidemiological studies, such as those on Överkalix and the Dutch Hunger Winter, link environmental exposure to health outcomes in later generations. The animal study on the other hand shows that certain reactions to stress could be inherited, which also gives us a molecular mechanism of response to stress (Dias & Ressler, 2014). However, the exact molecular bridge between animal models and human epidemiology remains unclear and requires further

investigation. These studies therefore give a strong basis for designing our own experiment, one that addresses the aspects missing from earlier work and could help confirm these findings in humans.

References

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