DEVELOPMENTAL TRAUMA AND THE ROLE OF EPIGENETICS

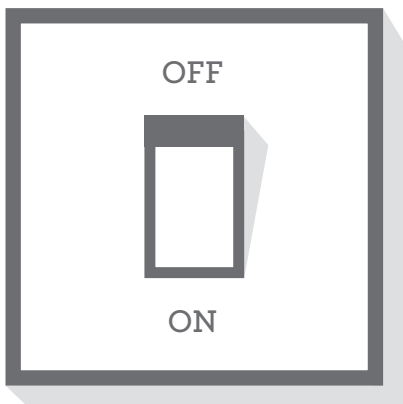
NIKKI KIYIMBA DEMONSTRATES HOW THE NEW FIELD OF EPIGENETICS PROVIDES FASCINATING INSIGHTS INTO THE DEBATE ABOUT THE RELATIONSHIP BETWEEN NATURE AND NURTURE

We are all familiar with the ongoing 'nature versus nurture' debate, as we strive to understand how much of human behaviour is predetermined through genetic coding and how much of it is the result of environmental influences. Epigenetics is a whole new phase of biological science that demonstrates to us the influence of environmental factors on the way that genetic DNA coding is expressed. The word 'epigenetics' was originally coined by Waddington[1] in 1942, and literally means 'on top of' genetics. Epigenetic changes are modifications of DNA, which occur without any alteration to the underlying DNA sequence, and can control whether a gene is turned 'on' or 'off'. Genetic expression therefore has been described using the metaphor of a light switch, as a gene is only activated when 'turned on' by the environment.[2] Waddington,[3] who started his work by studying fruit flies, noticed that when the flies were subjected to unusual circumstances, modifications occurred at a genetic level in their wing structures. Although these changes were acquired characteristics, he discovered that the changes actually became assimilated by the genotype. Importantly, unlike genetic mutations, these genetic changes are potentially reversible.[4]

Some of the more recent experiments in the field of epigenetics have been laboratory studies in which mice with the same genetic blueprint were exposed to different environmental conditions. The experiments were designed to examine the environmental impact on the DNA of the mice. Even though mice with identical DNA were kept in exactly the same environment and fed on exactly the same diet, some mice became larger and yellow coloured while other mice remained smaller and darker coloured.[5] The only difference between the two sets of mice was in what their mothers ate during pregnancy. In the case of the healthier brown baby mice, the mother mice were given methyl donor food supplements (folic acid, betaine, vitamin B12 and choline). These important studies have been quite revolutionary in bringing epigenetics to the forefront of our attention, by showing that maternal nutrition can have a huge impact on the physical development of offspring, due to epigenetic influences.

This phenomenon has also been researched in humans. One of the classic studies was conducted following the 'Dutch Hunger Winter'. Between the beginning of November 1944 and the late spring of 1945, there was a famine in Holland. Studies of individuals who were conceived during the famine indicated that they were at increased risk of developing schizophrenia, depression, heart disease, cognitive deficits and diabetes.[6] These studies showed that nutritional deprivation in human mothers appeared to have a significant impact on the children born following this period of deprivation.

In order to understand how genes are temporarily affected by such factors, we need to think briefly about the biological processes involved. The two primary mechanisms that happen in epigenetics are 'histone modification' and 'DNA methylation'. In the first of these, the double helix of DNA strands are tightly coiled around proteins called histones.



It is the spacing between these histones that determines how well the DNA strand can be read. Where DNA strands are bunched together around histones, the DNA strands cannot be as easily read as in the strands where histones are more spaced out. In the second mechanism, chemicals called methyl groups attach to DNA strands, thus blocking parts of them from being read. Usually when methylation of certain genes occurs, those genes will be significantly limited in their expression.

Methylation of DNA is an integral epigenetic aspect of the development and differentiation of cells, and can also be the starting point of several diseases.[7] Exposure to environmental stressors such as pollutants, alcohol and tobacco also has a detrimental impact on foetal DNA programming.[8] Research suggests that both the intrauterine environment and early postnatal experiences are critical windows for epigenetically mediated developmental trauma. One of the reasons for this is that the most significant opportunities for developmental plasticity occur during these periods, meaning that the child is most susceptible to the impact of chemical or social stresses.[9]

In addition to diet during pregnancy, another well-researched area has been the impact of maternal stress on the developing foetus. Fifty years of animal studies have shown that maternal stress during pregnancy can have long-term effects on the offspring, including learning deficits, altered immune function, more anxious behaviour, reduced attention, glucose intolerance and altered cardiovascular responses to stress. It is thought that cortisol crosses the placenta and may affect the foetus and disturb developmental processes. A review of the literature mostly suggests that prenatal stress or anxiety is associated with raised basal cortisol or raised cortisol reactivity in the offspring.[10] Encouragingly, some research has shown that a mild degree of stress during the prenatal period can actually increase the baby's mental and motor development.[11] However, it seems that higher levels of stress during pregnancy can potentially have a lasting adverse impact on the child.

A few high profile studies of international disasters, including 9/11,[12] Chernobyl[13] and a Canadian ice storm,[14] have examined the effects of acute stress on pregnant mothers and the subsequent impact on their children. Project Ice Storm studied 89 children whose mothers were pregnant during a natural disaster that occurred in January 1998 in the Canadian province of Quebec, which resulted in power losses for three million people for up to 40 days. Findings indicated that children exposed to this maternal stress during pregnancy had lower cognitive and language abilities at five-and-a-half years of age compared to children of mothers who had not been caught in the ice storm.[13]

Clearly, in-utero stress can have a detrimental impact on the physical, cognitive and psychological development of the unborn child and may lead to behavioural problems or even the development of mental illness. In addition to natural disasters, there are also more common sources of antenatal stress.

One of these is the experience of domestic violence. Research focused specifically on the impact of this, which was conducted by Radke and colleagues,[15] indicated that there were epigenetic modifications to the DNA of one of the cortisol receptors in the children of mothers who had experienced interpersonal violence while they were pregnant. Specifically, they found that methylation of the glucocorticoid receptor to which cortisol binds was influenced by the mother's experience of domestic violence during pregnancy.

Essentially this means that what began as 'acquired characteristics' can sometimes be inherited. It is possible that there is an evolutionary benefit for intergenerational epigenetic transfer. For example, children of prenatally undernourished fathers were found to be heavier or even obese in comparison to children of fathers who had not been undernourished.[20] This study suggests that it may be an evolutionary quirk that means that, in some cases of deprivation, genetic modification is passed on to future generations to better their chances of survival.

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There are many potentially traumatic events that can impact a child during their early life. These are collectively referred to as 'adverse childhood experiences' (ACEs) and include emotional, physical or sexual abuse, emotional or physical neglect and household dysfunction (including domestic violence, substance misuse, parental separation, incarceration of a family member or mental health difficulties in household members). These adverse events have been found to trigger detrimental effects of traumatic stress both on the child's developing neural networks and on the neuroendocrine systems that regulate them.[16] For example, there is evidence from post-mortem examinations that, when child abuse occurs, the epigenetic profile of the adult brain is altered and there are changes in the hippocampal glucocorticoid receptor.[17]

Although it may seem that the picture is already bleak enough, a further development in epigenetic research has found that changes to the structure of the DNA can actually be passed down from the mother or the father[18] and may even persist across multiple generations, being passed on from grandparents to grandchildren.[19]

The most optimistic aspect of this new knowledge about how the environment and the genetic make-up of an individual interact is that we now understand that DNA is not fundamentally or irrevocably changed. Rather, the DNA undergoes 'reversible' modifications in the way that it is read.[10] Thus, it may be possible to overturn the negative effects from in-utero and early childhood environmental stressors. The main thrust of research into this possibility is now focused strongly on how epigenetic changes can be altered. For example, drug companies are working on developing treatments that can modify the epigenetic imprints that contribute to disease development.

It is known that the brain retains its ability for self-renewal throughout life through the process of 'neurogenesis'. This is a kind of neuroplasticity that involves the growth of new neurons.[21] Adult neurogenesis is linked to hippocampal functioning, including learning and memory, and anxiety regulation. The hippocampus plays a central role in managing the autonomic nervous system, as well as facilitating the organisation of memories, and structural plasticity plays an important role in the way that the hippocampus functions. There are several ways that plasticity occurs: division (cell proliferation), selection (cell differentiation) and the maintenance of new neurons (cell survival). While stress has the negative impact of inhibiting neurogenesis by lowering cell proliferation, there are simple practical ways to improve neurogenesis. Firstly, physical exercise is known to activate the hypothalamic–pituitary–adrenal axis (HPA axis) and increase glucocorticoid levels, which in turn enhances neurogenesis. Other ways to improve neurogenesis are environmental enrichment, learning and rewarding social experiences. For example, in cases of childhood maltreatment, environmental interventions in the form of social support may prevent the development of depression.[22]

Importantly, there are also those in the field of counselling and psychotherapy who are applying these advances in our understanding of the neurology of trauma to talking therapy. For example, Feinstein and Church argue that counselling works on a neurological level by changing gene expression and that 'psychotherapeutic interventions … are effective in modulating the expression of genes'.[23] One reason for their effectiveness may be the close interaction of emotions and gene expression,[24] meaning that changes in cognitions, affect and behaviour correlate with gene modifications.[23] For example, researchers have found links between laughter and gene expression.[25] A study that assessed the effectiveness of therapies designed to enhance the relaxation response, such as meditation, breathing exercises, progressive muscle relaxation and guided imagery, also found both short- and long-term changes to specific gene expression.[26]

Through counselling, new neural pathways are created and healthier cognitions can in turn positively affect genes.[27] Epigenetics may lead us to a better understanding of how empathic attunement can promote neuroplasticity and thus, potentially, genetic change.[27] However, as Lipton[3] has explained, for this processing to be effective, the client's conscious thoughts and unconscious core beliefs need to be in harmony. The counsellor's role therefore can be to help the client to bring the unconscious into consciousness.[27]

Some researchers are now considering the role of psychotherapy in reversing the negative effects of epigenetic change. For example, one of the characteristics of post-traumatic stress disorder (PTSD) is increased glucocorticoid receptor sensitivity,[28] and it has been found that glucocorticoid-related genes are subject to environmental regulation throughout life.[29] A recent study of veterans diagnosed with PTSD concluded that, as psychotherapy is intrinsically an environmental influence, it is likely that it can be an influential factor in altering epigenetic states.[12] As Behm[27] has asserted, the mind and body need to be treated together, and 'the science of epigenetics has profound ramifications for all in the healing professions including physicians and counsellors'.[20] Therefore, increasing dialogue and sharing knowledge across the fields of neuroscience and psychotherapy can potentially help us to understand the complexities of interactions between mental wellbeing and biological mechanisms.[30]

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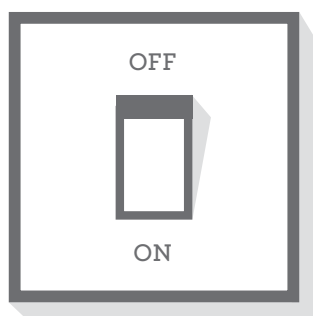

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