Epigenetics – a cause for optimism?

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Might it someday be possible to prevent a person developing mental illness? What would be needed to achieve such a goal? First, probably, an early marker that the person was at risk, and secondly, an effective intervention, perhaps best targeted at the underlying mechanisms. Until recently, neither of these conditions seemed likely to be met.

The recognition that aspects of development, especially before birth, are associated with later risk of non-communicable diseases (NCDs) has, however, opened up new possibilities. 1 What is novel is the establishment of specific components of the developmental environment that lead to increased likelihood of disturbed responses to later challenges. The role of maternal nutrition in pregnancy was demonstrated from observations that offspring of women who were subjected to famine in early gestation during the Dutch Hunger Winter of 1944/5 were more likely to develop a range of affective and other disorders 40–60 years later. 2

Animal studies have revealed an interaction between prenatal undernutrition and altered hypothalamic-pituitary-adrenal stress responses of the offspring, 3 and effects mediated by this axis can be affected by maternal behaviour. 4 Similar effects can be observed in wild animal populations. 5,6 These studies give insights into the long-term effects in human offspring of stressful events before birth, such as the Holocaust or the World Trade Center attack. 7,8

The second area in which advances have been made concerns epigenetics – the processes by which the environment can effect gene expression and function, to produce developmental plasticity. 1 Where plasticity affects neuroendocrine control processes such as those involved in stress responses, the long-term effects on an individual’s responses to later stressful challenges can be detrimental to their mental health. 9

Epigenetic markers induced before birth can be measured in early life, for example in umbilical cord or cord blood. Initiatives to characterise them are leading to potentially valuable biomarkers, not only of how the developmental environment affected the developing foetus, but also as predictors of later risk of a range of NCDs. Moreover, they give insights into underlying mechanisms. 4 When the period of developmental plasticity extends after birth, the opportunity to reverse the earlier epigenetic changes exists, and the biomarkers may serve to monitor the efficacy of such intervention. Coupling this to the promising effects of personalised support for childhood development may be very effective. 10

The elucidation of epigenetic processes forms an essential component of the field of developmental origins of health and disease (DOHaD). 11 DOHaD research challenges the view that risk of NCDs, including mental illness, is the result of an inherited predisposition coupled with unhealthy adult lifestyle behaviours, which are very difficult to change. It shows how risk of disease can be transmitted across generations, but also that aspects of the developmental environment which induce epigenetic changes are modifiable. The underlying social and wider issues may not be easy to tackle, but now that we know that change is possible there is a cause for optimism.

Declaration of interests

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References