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Epigenetics and stress

Baby blues

A mother's stress while she is pregnant can have a long-lasting effect on her children's genes

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RESEARCHERS have known for years that children whose mothers were chronically stressed during pregnancy—by famine, anxiety, the death of a relative or marital discord, for instance—show higher-than-normal rates of various psychological and behavioural disorders when they are adults. They have also known for a long time that those brought up in abusive environments often turn out to be abusive themselves.



The second of these observations is usually put down to learning. The reason for the first has remained unclear. A study just published by Axel Meyer, Thomas Elbert and their colleagues at the University of Konstanz in Germany, however, points to a phenomenon called epigenetics as the likely answer. And if Drs Meyer and Elbert are right, it also suggests an alternative explanation for the inheritance of abusiveness.

Epigenetics is a type of gene regulation that can be passed from a cell to its daughters. The most common mechanism is methylation. This attaches methyl groups (a carbon atom and three hydrogens) to either adenine or cytosine, two of the four chemical bases that form the alphabet of DNA, depending on the gene involved. The consequence is to inactivate the gene being methylated.

In the case of stress, previous studies have suggested that methylation of the gene which encodes glucocorticoid receptors is important. Glucocorticoid receptors relay signals from stress hormones in the blood into cells. In particular, they do so in those regions of the brain that control behaviour. Newborns whose mothers suffered from depression while they were pregnant are known to have more highly methylated glucocorticoid-receptor genes than others. The same is true of children who were abused when young. In infants, the level of glucocorticoid-receptor methylation is correlated with the release, in response to stress, of higher-than-normal amounts of stress hormones. And in rats, such methylation makes young animals especially sensitive to stress, and also fearful of novelty.

What has been unclear until now, however, is how long such effects persist. Dr Meyer's and Dr Elbert's study, published in *Translational Psychiatry*, offers a clue.

Troubled teens

Their team examined the methylation of the glucocorticoid-receptor gene in a group of children ranging in age from ten to 19 years, and in those children's mothers. The researchers also used a psychological survey to try to determine which of the mothers had been physically or psychologically abused before, during or after pregnancy. They found that women abused

during pregnancy were significantly more likely than others to have a child with methylated glucocorticoid-receptor genes. By contrast, abuse before or after pregnancy resulted in no such correlation. Nor was the mother's own methylation affected by violence towards her. Taken together, these results suggest that glucocorticoid-receptor-gene methylation happens in the fetus in response to a mother's stress, and persists into adolescence.

This has implications for those adolescents' long-term health. Dampened glucocorticoid-receptor-gene activity has been shown to increase the risk of obesity, of depression and of some autoimmune diseases. It also makes people more impulsive and aggressive—and therefore, if male, more likely to abuse the pregnant mothers of their children, thus perpetuating the whole sorry cycle.

Why, in light of such negative effects, have humans evolved to be programmed this way while still in the womb? Part of the answer is probably that not all the negative consequences would have shown up at the time the mechanism was evolving. Obesity, for example, is rare in a state of nature. The other part is that some of the consequences probably have a positive effect. If a mother lives in an environment where fear-inducing experiences are common, say, giving her offspring a sensitivity to fear may be no bad thing.

What can be done with such knowledge is unclear. Drugs that demethylate DNA are under development, but are still some way from approval—and, in any case, interfering with epigenetics, which is a widespread mechanism of gene regulation, is a drastic approach. The research might, though, point to the period when intervening to stop abuse will have the greatest effect. Then again, such intervention is always desirable, for the sake of both mother and child.

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