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Pregnant 9/11 survivors transmitted trauma to their children

The emerging field of epigenetics shows how traumatic experiences can be transmitted from one generation to the next

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For New Yorkers, the events that transpired on the morning of 11 September, 2001 must have seemed like a nightmare. Immediately after the attack on the World Trade Centre that day, psychologists predicted that a wave of trauma would sweep across the country. Although this prediction turned out to be wrong, it is estimated that some 530,000 New York City residents suffered from symptoms of post-traumatic stress disorder (PTSD) in the months following the attack.

Among the tens of thousands of people directly exposed to the World Trade Centre attack were approximately 1,700 pregnant women. Some of these women went on to develop symptoms of PTSD, and some of the children have inherited the nightmare that their mothers experienced on that day.

Within weeks of the attack, researchers at the Traumatic Stress Studies Division at the Mount Sinai Medical Centre in New York were inundated with telephone calls from people who had been traumatised by the event, including pregnant women. Rachel Yehuda, professor of psychiatry and neuroscience in charge of the division, set out to investigate how these women's experiences might affect their children.

To do so, Yehuda and her colleagues performed a longitudinal study. They recruited 38 women who were pregnant on 9/11 and were either at or near the World Trade Centre at the time of the attack, some of whom went on to develop PTSD. The researchers took samples of saliva from them and measured levels of the stress hormone cortisol.

They found that those women who had developed PTSD following exposure to the attacks had significantly lower cortisol levels in their saliva than those who were similarly exposed but did not develop PTSD. About a year later, the researchers measured cortisol levels in the children, and found that those born to the women who had developed PTSD had lower levels of the hormone than the others. Intriguingly, reduced cortisol levels were most apparent in those children whose mothers were in the third trimester of pregnancy when they were exposed to the attack.

Following up these findings, Yehuda and her colleagues have also shown that the children of women who were traumatised as a result of 9/11 subsequently exhibit an increased distress response when shown novel stimuli. Again, this was related to the stage of pregnancy - those with the largest distress response were the ones born to mothers who were in their second or third trimester when exposed to the World Trade Centre attacks.

How might the traumatic experiences of a pregnant woman be transmitted to her unborn children? Research published over the past 10 years or so suggests that this probably occurs by epigenetic mechanisms. Epigenetics is the study of heritable changes in gene activity that are not due to changes in DNA sequence. Epigenetics reveals how genes interact with environmental factors, and has been implicated in many normal and abnormal brain functions.

A key study in this emerging field, published in 2004, showed that the quality of a rat mother's care significantly affects how its offspring behave in adulthood. Michael Meaney of McGill University and his colleagues found that rat pups that had been repeatedly groomed and licked by their mothers during the first week of life were subsequently better at coping with stressful and fearful situations than pups who received little or no contact.

They further showed that these effects are mediated by epigenetic mechanisms that alter expression of the glucocorticoid receptor, which plays a key role in the body's response to stress. Analysis of the pups' brains at one week old revealed differences in DNA methylation, a process by which DNA is chemically modified. Methylation involves the addition of small molecules called methyl groups, consisting of one carbon and three hydrogen atoms, to specific sites in the DNA sequence encoding a gene.

Specifically, pups that received high levels of grooming and licking had higher levels of methylation within regions of DNA that regulate the activity of the glucocorticoid gene. These modifications open up the chromosomal region containing these regulatory regions, so that the molecular machinery that synthesises proteins can gain access to the receptor gene sequence. By contrast, these epigenetic markers, as they are known, were not seen in the "low maternal care" pups, and consequently gluocorticoid receptor levels were reduced in these animals' brains.

Similar mechanisms probably account for the transmission of trauma from mother to unborn child. More recently, Yehuda and her colleagues examined gene expression patterns in 40 individuals who were similarly exposed to the World Trade Centre attacks, and identified 16 genes that are differentially expressed between those with and those without PTSD.

Several of these genes regulate the function of the glucocorticoid receptor and two - FKBP5 and STAT5B - directly inhibit its activity. Expression of both these genes is reduced in individuals with PTSD, and this may contribute to the high levels of glucocorticoid receptor activity that is consistently observed in the condition. Others have shown that variations in FKBP5 are associated with the severity of PTSD symptoms in individuals who suffered child abuse.

Yehuda has obtained similar results in the adult offspring of Nazi holocaust survivors, and is currently trying to identify genetic variations and epigenetic markers associated with PTSD in combat veterans. The precise mechanism by which traumatic experiences are transmitted from one generation to the next is still not known, but a picture is beginning to emerge.

Yehuda's work establishes low cortisol levels as a risk factor for developing PTSD and, when taken together with the animal studies, suggests that traumatic experiences can leave epigenetic marks that alter the stress response in offspring. Epigenetic factors combined with genetic variations could also explain why some people are more susceptible to stress than others, and why some of those exposed to the World Trade Centre attacks went on to develop PTSD while others did not.

In the animal study led by Meaney, the epigenetic modifications and the changes in glucocorticoid receptor expression associated with them were observed in the hippocampus, a brain region that is essential for learning and memory formation. It is, therefore, possible that epigenetic markers are laid down during the formation of traumatic memories.

Last month, researchers from the University of Pennsylvania reported that epigenetic markers can be transmitted through two generations of mice, suggesting that children who inherited the nightmare of the World Trade Centre attack from their mothers while in the womb may in turn pass it on to their own children.

References:

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- This article was corrected on Friday 9 September 2011. There was a typo in the first paragraph.