Medical Xpress

Stress during pregnancy can be passed down through generations

August 7 2014

To better understand problems during pregnancies today, we should look to the experiences of our ancestors, research published in the open access journal *BMC Medicine* suggests. Scientists investigating pregnancies in four generations of rats show that inherited epigenetic effects of stress could affect pregnancies for generations.

Researchers from the University of Lethbridge in Canada wanted to investigate how preterm births are influenced by stress. Preterm birth is one of the leading causes of neonatal death and can lead to health problems later in life. They examined the length of pregnancies in rats because in general there is very little variation between them.

A first generation of rats were subjected to stress late in pregnancy. The following two generations were then split into two groups that were either stressed or not stressed. The daughters of stressed rats had shorter pregnancies than the daughters of those who had not been. Remarkably, the grand-daughters of stressed rats had shorter pregnancies, even if their mothers had not been stressed.

As well as shorter pregnancies, the rats whose grandmothers and mothers experienced stress displayed higher glucose levels than the control group. In addition, rats whose grandmothers or mothers who were stressed weighed less.

Gerlinde Metz, senior author of the article, says: "We show that stress across generations becomes powerful enough to shorten pregnancy length in rats and induce hallmark features of human preterm birth. A surprising finding was that mild to moderate stress during pregnancy had a compounding effect across generations. Thus, the effects of stress grew larger with each generation."

The researchers believe that these changes are due to epigenetics - the arrangement and expression of our genes. In most cases this refers to DNA methylation of the nucleotide base pairs. In this study the researchers believe the epigenetic changes are due to microRNA (miRNA) - non-coding RNA molecules that play a role in regulating gene expression.

Gerlinde Metz says: "Previous epigenetic studies have mainly focused on inheritance of DNA methylation signatures. What we didn't know was whether microRNAs, which are important biomarkers of human disease, can be generated by experiences and inherited across generations. We have now shown that maternal stress can generate miRNA modifications with effects across several generations. I think this is an interesting feature of our manuscript."

Further work needs to be done to understand the mechanisms that generate these epigenetic signatures and how they are passed down from generation to generation. With more knowledge of these mechanisms it may be possible to predict and prevent preterm pregnancy but also other diseases.

Gerlinde Metz says: "Preterm births can be caused by many factors, in our study we provide new insights into how stress in our mothers, grandmothers and beyond could influence our risk for pregnancy and childbirth complications. The findings have implications outside of pregnancy, in that they suggest that the causes of many complex diseases could be rooted in the experiences of our ancestors. When we better understand the mechanisms of inherited epigenetic signatures, we can predict disease risk and potentially reduce the future risk of illness."

More information: Ancestral Exposure to Stress Epigenetically Programs Preterm Birth Risk and Adverse Maternal and Newborn Outcomes Youli Yao, Alexandra M Robinson, Fabiola CR Zucchi, Jerrah C Robbins, Olena Babenko, Olga Kovalchuk, Igor Kovalchuk, David M Olson and Gerlinde AS Metz *BMC Medicine* 2014, 12:121. www.biomedcentral.com/1741-7015/12/121

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