# Study shows moms may pass effects of stress to offspring via vaginal bacteria and placenta

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Pregnant women may transmit the damaging effects of stress to their unborn child by way of the bacteria in their vagina and through the placenta, suggest new findings from two animal studies presented by researchers at the University of Pennsylvania at Neuroscience 2013, the annual meeting of the Society for Neuroscience.

Stresses felt by mothers during pregnancy have been shown to affect offspring neurodevelopment and increase the risk for disorders such as autism and schizophrenia, but the mechanisms by which it can reprogram the developing brain are not clear.

As a newborn passes through the birth canal, the microbiome of a mother's vagina ends up in the offspring's gut. In the first study, the team, led by Tracy L. Bale, PhD, Professor of Neuroscience in the Perelman School of Medicine, Department of Psychiatry and the School of Veterinary Medicine Department of Animal Biology at Penn, found that changes in the microbiome produced by stress in pregnant mice altered the microbe population in the newborn's gut and correlated to changes in the developing brain.

Using targeted approaches in mice, the researchers determined that early prenatal stress affected both the maternal and offspring levels of lactobacillus, a lactic acid-producing bacteria associated with brain neurochemistry. It has been demonstrated that throwing off those levels can affect neurodevelopment.

The team then observed changes in gene expression in the hypothalamus in offspring of the mice that correlated with levels of lactobacillus. Many of these genes play a critical role in development and brain function.

"For the first time, we've shown how stress can change the microbiome in the vagina and impact the microbiome of her offspring's gut, and that may, in part, ultimately affect their brain function and neurodevelopment," said Bale. "This mechanism could help us better understand how it may predispose individuals to neurodevelopmental disorders."

In a parallel animal study, Bale and colleagues were looking for predictive biomarkers of maternal stress and found that a specific protein in the placenta, OGT, may have implications for brain development in offspring. The single enzyme is known as O-linked-N-acetylglucosamine transferase or "OGT," which is important in a wide variety of regulatory functions, including development.

The researchers found that placentas associated with male mouse pups had lower levels of OGT than the placentas associated with female pups, and levels of OGT in the placenta were even lower when their moms were stressed.

The team then used transgenics to directly manipulate placental OGT levels similar to the effect that maternal stress has. That way, they could ask if any of the effects of mom's stress on brain development and function were related to this placental gene. What they found was fascinating—when these babies became adults, they were smaller and more sensitive to stress, very similar to the offspring from the stressed moms.

"Since lower levels were associated with stress, these results suggest that placental OGT may provide a protective role during pregnancy," said Bale. "These data also suggest that OGT may serve as a biomarker for a range of neurodevelopmental disorders in children, as we have previously shown similar regulation of this

gene in human placental tissue."

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