Do children inherit parents' stressful experiences?

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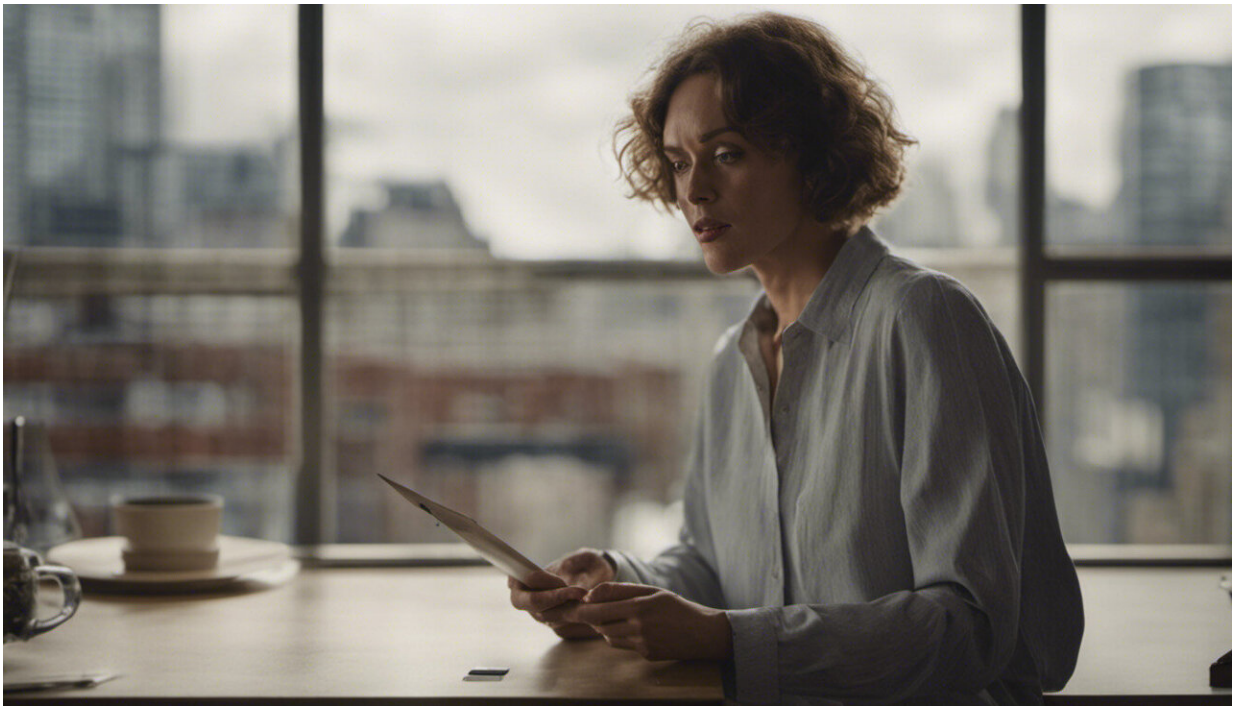

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Most of us learned in high school that people get half their genes from their father and half from their mother. That's true, but it turns out the way parents contribute to their offspring's genetics is more complicated—and more intriguing.

Tufts School of Medicine researcher Larry Feig is enrolling participants in a study with Boston IVF to see if the effects of men's positive or negative experiences can be passed across generations because of altered sperm.

Scientists are discovering that a parent's experiences can lead to changes in gene expression that are encoded in the sperm or egg and passed to offspring. In other words, there is a way in which offspring inherit the experiences of their parents. This is different than inheriting genes for brown or blue eyes. It's more like inheriting genes that are switched on or off for the purpose of being better adapted to a particular environment.

Feig is helping to illuminate how changes in gene expression, called epigenetic changes, can be passed down. Feig says, "You inherit the experiences of your ancestors? How could this be? And why?"

The "why" could be that genetic expression based on parental experience helps set the stage for successful offspring. For example, mice raised in cold environments pack on a type of fat called brown fat to keep themselves warm. Their offspring are born with extra brown fat, presumably giving them a survival boost in cold temperatures.

"The idea is that under normal circumstances, it's a good thing," Feig says. "Like any other regulatory system, if it's in excess, it could cause harm." Regarding the latter, Feig is interested in whether childhood trauma might result in parents passing along epigenetic changes that make their children more susceptible to psychiatric disorders.

Feig has shown that male mice exposed to social stress (in the form of frequent rearranging of social groups) have different levels of molecules called microRNA in their sperm. After the sperm has fertilized the egg, these microRNA molecules give directions about how genes are

expressed in the developing embryo. In the sperm of the stressed mice and early embryos derived from them, Feig found that two specific microRNA molecules occur at much lower levels than those from non-stressed mice.

The female offspring of these stressed mice show more anxious behavior than normal. The male offspring don't; however, they do have the same changes in their sperm, even though they weren't stressed themselves. And their female offspring are anxious.

Feig followed up with a small pilot study in humans and found that men with adverse childhood experiences (such as physical or emotional abuse or neglect) had decreased levels of the same microRNA in their sperm. "We saw changes in men's sperm that matched the changes in mice sperm," he says. "It was a striking result."

Now Feig is working on a much larger study in humans to confirm those findings and to delve deeper.

In the new study, participating men will be asked not only about adverse childhood experiences, but also about adult adverse experiences such as those associated with PTSD, as well as their current levels of depression and anxiety. In addition, they will be asked about the sorts of positive childhood experiences that have been shown to mitigate early trauma. Feig wonders whether those positive experiences might boost the levels of the two microRNA molecules in sperm. This seems to be the case for mice, according to studies by other researchers.

In addition, the new study brings in another generation—the men's fathers. This will help illuminate the question of whether stress or trauma in one generation shows up in stress-related sperm changes in the next generation.

In the past, Feig has mostly worked with mice and cells, not humans. While making the transition, he benefited from his daughter's experience. Emily Feig, is a clinical psychologist and researcher at Massachusetts General Hospital and assistant professor at Harvard Medical School, who was introduced to research in the Tufts Summer Scholars program. She now studies novel ways to improve health behaviors in people with obesity.

Feig plans to enroll about 300 participants, and to do so, he is collaborating with Boston IVF, a clinical fertility center that also includes a fertility research program headed by Scientific Director Denny Sakkas. Tufts student Aidan Chen, is helping with enrollment and consent at Boston IVF, where he was interning when Feig began his study.

For Feig's study, Chen reaches out to men who come to the center about fertility issues, explaining the study and inviting them to participate. "I've learned a lot about how to communicate efficiently and empathetically with patients who are coming in," he says. "It's really important to be considerate because these patients are coming for care first and foremost. The research doesn't impede that process in any way."

Chen has also started working in Feig's lab under the tutelage of postdoc Alexandre Champroux who is heading this project.

The samples include not only sperm, but saliva as well. Feig and members of his lab are analyzing the saliva to see if it shows the same fluctuations in microRNA as sperm. If so, perhaps in the future, a simple saliva test could identify people whose microRNA levels indicate that their stressful experiences put them—or their future offspring—at risk for mental illness.

"If certain microRNA changes make the next generation susceptible to psychiatric disorders," he says, "you might be able to reverse those changes, by therapy, meditation or antidepressants, before people have kids. It's much easier to change epigenetics than genetics, because epigenetic regulation of genes, including those that control sperm microRNA levels, responds to the environment."

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