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Study finds that fear can travel quickly through generations of mice DNA

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A newborn mouse pup, seemingly innocent to the workings of the world, may actually harbor generations' worth of information passed down by its ancestors.

In the experiment, researchers taught male mice to fear the smell of cherry blossoms by associating the scent with mild foot shocks. Two weeks later, they bred with females. The resulting pups were raised to adulthood having never been exposed to the smell.

Yet when the critters caught a whiff of it for the first time, they suddenly became anxious and fearful. They were even born with more cherry-blossom-detecting neurons in their noses and more brain space devoted to cherry-blossom-smelling.

The memory transmission extended out another generation when these male mice bred, and similar results were found.

Neuroscientists at Emory University found that genetic markers, thought to be wiped clean before birth, were used to transmit a single traumatic experience across generations, leaving behind traces in the behavior and anatomy of future pups.

The study, published online Sunday in the journal Nature

Neuroscience, adds to a growing pile of evidence suggesting that characteristics outside of the strict genetic code may also be acquired from our parents through epigenetic inheritance. Epigenetics studies how molecules act as DNA markers that influence how the genome is read. We pick up these epigenetic markers during our lives and in various locations on our body as we develop and interact with our environment.

Through a process dubbed “reprogramming,” these epigenetic markers were thought to be erased in the earliest stages of development in mammals. But recent research — this study included — has shown that some of these markers may survive to the next generation.

"When I was in school, this was against Darwin — it was ridiculed," said University of Pennsylvania neuroscientist Christopher Pierce, who was not involved in the study but previously discovered an epigenetic inheritance related to cocaine. Male rats whose fathers were exposed to cocaine chose to ingest less of the drug than those rats whose fathers never took cocaine.

Pierce says he believes this is an adaptive effect — because cocaine is a toxin, the fathers passed down information to their pups that would help them survive and avoid the substance.

In the past decade, the once-controversial field of epigenetics has blossomed. But proving epigenetic inheritance can be a daunting, needle-in-a-haystack undertaking. Researchers need to measure changes in offspring behavior and neuroanatomy, as well as tease out epigenetic markers within the father’s sperm.

The DNA itself doesn’t change, but how the sequence is read can vary wildly depending on which parts are accessible. Even though all the cells in our bodies share the same DNA, these markers can silence all the irrelevant genes so that a skin cell can be a skin cell, and not a brain cell or a liver cell.

"This fine-tuning of gene expression occurs by epigenetics," said postdoctoral researcher and study author Brian Dias of Emory's Yerkes National Primate Research Center.

For instance, methyl molecules can bind to the sequence and block access to genes. Other proteins called histones act like spools for the 2 meters of DNA, about 6.5 feet, crammed into every tiny nucleus in our bodies. Some areas are so tightly wound up that those parts unreadable.

Dias combined his interest in animal development with neurobiologist Kerry Ressler's focus on the mechanisms of fear learning. They taught two groups of male mice to fear odors by zapping their feet with an electric shock every time they blew scented air into their cages. The experimental group became afraid of cherry blossoms with a hint of almond, and the control group feared alcohol.

After three days of fear conditioning, the cherry blossom mice later reproduced. The resulting offspring, having grown to adulthood, had a heightened jumpiness to the cherry blossom smell, despite never having been exposed to it. They had no overreaction to alcohol.

They could also pick up on lesser amounts of cherry blossom in the air, which reflected their changes in olfactory and brain anatomy. When Dias stained only the cherry-blossom-detecting olfactory neurons blue, he saw significantly more of them coding for that smell as compared with the control mice.

The researchers also artificially inseminated females using the sperm from the original fear-conditioned mice, to attempt to get rid of any possible socially transmitted effects between the fathers and the females. The results were the same, suggesting epigenetic inheritance rather than environment.

The findings were also verified by comparing the epigenetic markers on the DNA of sperm, specifically on the gene responsible for detecting cherry blossoms. On the sperm of the cherry-blossom-fearing mice, there was less of the methylation that can silence genes, possibly pointing to a mechanism of how the information got passed down.

Pierce was impressed by the thoroughness of Dias's and Ressler's study.

"It's a compelling finding," he said. "The fact that epigenetic changes happen in mammals is just amazing."

Does this mean we as humans have also inherited generations of fears and experiences? Quite possibly, say scientists. Studies on humans suggest that children and grandchildren may have felt the epigenetic impact of such traumatic events such as famine, the Holocaust and the Sept. 11, 2001, terrorist attacks.

"Those are really powerful studies — unfortunately so, since the effects have been detrimental to subsequent generations," Dias said. But because environmental factors for human subjects can't be controlled, it is difficult to parse out the effects of epigenetics alone.

There are some who are skeptical of even mammal studies of epigenetics, and Dias believes they are rightly so since the field of epigenetics is still relatively new.

“We’re still scratching the surface,” he said.

Kim is a freelance science journalist based in Philadelphia.