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Abuse Changes Children's Genes | NOVA | PBS

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9–12 minutes

Over 50 kids showed up at the Child Emotion Lab in Madison, Wisconsin. Most of them grew up in typical households. They were there because their parents just happened to see an ad in the city's buses or newspapers. But about a third of them were recruited for the study there because their childhoods had been anything but normal. These kids, according to records kept by Child Protective Services, had been abused.

For abused children, that trauma is just the beginning. Most will likely struggle well into adulthood. Living with an abusive parent has increased their risk for depression and other psychological problems while decreasing their chances of successfully maintaining close relationships. Even physical ailments, like type 2 diabetes and heart disease, are more likely in adults who were abused as kids. Early abusive experiences can leave a stubborn imprint on those children's brains and bodies, and Seth Pollak, a professor at the University of Wisconsin and head of the study, wanted to know how, exactly, abuse was changing these children's bodies on a cellular level.

"We know about these difficulties, but we've had a really hard time

understanding why. What's getting under people's skin?" Pollak says. "Why are they still having the social difficulties and the emotional difficulties because of something that happened when they were two?"

Increasingly, scientists are coming to realize that people's experiences exert a strong influence on their biology by silencing genes or turning them back on, significantly changing the way a cell functions without changing its DNA sequence. It's a phenomenon known as epigenetics. "Epigenetics makes the genes tick," explains Moshe Szyf, a professor of genetics and pharmacology at McGill University. Epigenetic changes modify DNA to keep genes from being expressed, and they can explain dramatic differences between cells with identical DNA—for example, how stem cells can turn into either liver cells or heart cells, or why only one of a set of identical twins gets cancer. It's also, Pollak found, why children who grow up in abusive homes have physical and psychological problems that haunt them well into adulthood.

Stress, Abuse, and Genetics

Since he was in graduate school, Pollak has been interested in the way traumatic childhood experiences might change the brain. But, he says, the people studying those at-risk children were mostly social workers. Neuroscientists were interested in the role of brain biology in problems like depression and schizophrenia, but "when you started talking about really messy social problems like child abuse and poverty, they would look at me like, well how are you ever going to study that?" Pollak says. "They were different worlds."

The first hint that the worlds of child welfare and neuroscience could be unified was a 2005 study by Moshe Szyf and his colleagues at McGill University, which showed that rat pups raised by abusive mothers had epigenetic changes in a gene that helps rats—and humans—manage stress. This gene, called NR3C1, had a few extra methyl groups stuck to it: tiny quartets of carbon and hydrogen atoms that stick to DNA and derail the cellular machinery that translates genes into proteins. A methylated gene is still there, but it's muted.

Scientists knew that things like drugs or radiation could turn genes off in this way, but Szyf's experiment, Pollak says, "was the first demonstration that something like parenting, parental care, was flipping the switch." A few studies in humans also hinted that trauma might be turning this stress-management gene off, but there wasn't any direct evidence in children. That's what Pollak was determined to find.

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So Pollak's staff recruited those kids and their parents and walked the kids from the lab to a local hospital to get their blood drawn. When they checked each kid's DNA, they saw that, in the children with a history of abuse, NR3C1 was methylated, just as it had been in the rats—in fact, at the very same sites. That, Pollak thought, was remarkable. "It gives us a real window into understanding why people that are abused as children sort of have these lifelong problems."

NR3C1 codes for a receptor that senses a hormone called cortisol. "Cortisol is something that we produce in an emergency," Pollak

explains. That's because it prepares you to respond to a threat: when cortisol from the adrenal gland is sent flowing into the bloodstream, it ramps up blood sugar for a quick burst of energy, dials down energy-draining processes like digestion, growth, and immune function, and can reduce bleeding and inflammation if you're injured. University of Minnesota professor Megan Gunnar points out that, for children in abusive homes, who are in threatening situations every day, having more cortisol floating around isn't necessarily bad—at first. "You may need to remain vigilant more often. You may need to flip into vigilant state more easily. That's keeping you alive under harsh conditions, but it's also making it really hard for you to function."

Normally, cortisol molecules dock in receptors that are coded for by NR3C1 in the brain and white blood cells, which signals the body to calm down and return to its normal operating mode, and revives the immune system. But if NR3C1 is methylated, the body won't be able to produce enough receptors, hobbling its ability to regulate stress. The body can still produce cortisol, but without enough receptors, Pollak says, there's nothing to reign in the heightened state. "It's the brake that's not working."

When the body can't signal itself to calm down, the short term results are kids who, Pollak says, are "on alert all the time." They often misinterpret innocent behavior as threatening; they can be aggressive, and they struggle with change. The long-term results are the chronic psychological problems like anxiety and depression and chronic physical problems like heart disease and type II diabetes, which often surface years later in victims of childhood abuse.

Health Concerns

Pollak only looked at DNA from white blood cells, so his study couldn't tell whether these children have fewer receptors in their brains, a measure that can only be taken from deceased individuals (although the data from postmortem experiments on both rats and humans leads Pollak to believe that they do). But Szyf and Gunnar agree that the fact that these changes occur in the immune system is significant on its own. Having too few receptors for cortisol keeps the immune system from learning to manage inflammation and infections, helping explain why children in abusive homes seem to get sick more often, and are at a higher risk for chronic health problems.

Gunnar believes that this study is an important demonstration that epigenetic changes can link childhood trauma and long-term physical and emotional problems. "It's certainly a piece of the puzzle," she says, but cautions that, "It's not going to be the whole story." There are probably a lot of other genes that get methylated, and genes themselves and learned coping mechanisms also play a role in how kids respond to stress. Still, she agrees. "Changes in the epigenetics is going to be a big piece of the story."

For one thing, identifying NR3C1 methylation in abuse victims gives researchers a concrete way to measure the biological effects of abuse and to determine if treatments are working. "The main thing missing in behavioral intervention," Szyf says, "was objective measures to develop good protocols." Cortisol levels themselves aren't good diagnostic tests, because they fluctuate over the course of the day and are easily swayed by transient factors like illness or even laughter. The methylation Pollak discovered, while

not exclusively caused by stress, is a much more stable and useful measure.

Undoing the Damage

Fortunately for abused children, there's reason for hope. Szyf's experiments in rats suggests that NR3C1 isn't necessarily permanently silenced: when the abused pups were returned to nurturing mothers, the extra methylation disappeared. "The idea that these things aren't fixed is really encouraging," Pollak says.

Even kids from horrific backgrounds developed a rapport with the lab's staff.

To what extent methylation on these genes might be reversible in children, and what kind of interventions might help, Pollak says, "are just big questions that we don't have the answers to yet." But he's hopeful that, now that this epigenetic mechanism is known, "someone who is a really skilled expert clinician might have an aha! moment. And that's all it takes to kind of really reorient things to think about a different way to have an effective treatment."

What's encouraging, Pollak says, is that even kids from horrific backgrounds developed a rapport with the lab's staff, which has buoyed his optimism for developing treatments. "They want to talk to us, they want to tell us stories," he says. After making it through the blood draw, a lot of the kids bubbled over with pride.

"I would say honestly there are many days when we all kind of put our head in our hands and we can't, we just can't believe what has happened in these children's lives," Pollak admits. "But it motivates us; I mean, what's going on in these children's lives, it kind of keeps a fire under our ass not to be lazy, and we have to keep these studies going, because there are a lot of kids in need."

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