

## Can the legacy of trauma be passed down the generations?

Martha Henriques :: 26/03/2019



Our children and grandchildren are shaped by the genes they inherit from us, but new research is revealing that experiences of hardship or violence can leave their mark too.

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In 1864, nearing the end of the US Civil War, conditions in the Confederate prisoner of war camps were at their worst. There was such overcrowding in some camps that the prisoners, Union Army soldiers from the north, each had the square footage of a grave. Prisoner death rates soared.

For those who survived, the harrowing experiences marked many of them for life. They returned to society with impaired health, [worse job prospects and shorter life expectancy](#). But the impact of these hardships did not stop with those who experienced it. It also [had an effect on the prisoners' children and grandchildren](#), which appeared to be passed down the male line of families.

While their sons and grandsons had not suffered the hardships of the PoW camps – and if anything were well provided for through their childhoods – they suffered higher rates of mortality than the wider population. It appeared the PoWs had passed on some element of their trauma to their offspring.

But unlike most inherited conditions, this was not caused by mutations to the genetic code itself. Instead, the researchers were investigating a much more obscure type of inheritance: how events in someone's lifetime can change the way their DNA is expressed, and how that change can be passed on to the next generation.

This is the process of epigenetics, where the readability, or expression, of genes is modified without changing the DNA code itself. Tiny chemical tags are added to or removed from our DNA in response to changes in the environment in which we are living. These tags turn genes on or off, offering a way of adapting to changing conditions without inflicting a more permanent shift in our genomes.



The effects of trauma may echo down several generations, from a grandfather to their son and then to their grandson (Credit: Alamy/Getty Images/BBC)

But if these epigenetic changes acquired during life can indeed also be passed on to later generations, the implications would be huge. Your experiences during your lifetime – particularly traumatic ones – would have a very real impact on your family for generations to come. There are a growing number of studies that support the idea that the effects of trauma can reverberate down the generations through epigenetics.

For the PoWs in the Confederate camps, these epigenetic changes were a result of the extreme overcrowding, poor sanitation and malnutrition. The men had to survive on small rations of corn, and [many died from diarrhoea and scurvy](#).

“There is this period of intense starvation,” says study author Dora Costa, an economist at the University of California, Los Angeles. “The men were reduced to walking skeletons.”

## **The sons of PoWs had an 11% higher mortality rate than the sons of non-PoW veterans**

Costa and her colleagues studied the health records of nearly 4,600 children whose fathers had been PoWs, comparing them to just over 15,300 children of veterans of the war who had not been captured.

The sons of PoWs had an 11% higher mortality rate than the sons of non-PoW veterans. Other factors such as the father's socioeconomic status and the son's job and marital status couldn't account for the higher mortality rate, the researchers found.

This excess mortality was mainly due to higher rates of cerebral haemorrhage. The sons of PoW veterans were also slightly more likely to die from cancer. But the daughters of former PoWs appeared to be immune to these effects.

This unusual sex-linked pattern was one of the reasons that made Costa suspect that these health differences were caused by epigenetic changes. But first Costa and her team had to rule out that it was a genetic effect.



For some reason, the trauma seem to be most strongly passed from fathers to their sons (Credit: Alamy/Getty Images/BBC)

“What could have happened is that a genetic trait which enabled the father to survive the camp, a tendency toward obesity for example, was then bad during normal times,” says Costa. “However, if you look within families, there are only effects among sons born after but not before the war.”

If it were a genetic trait then children born before and after the war would be equally likely to show the reduced life expectancy. With a genetic cause ruled out, the most plausible explanation left was an epigenetic effect.

“The hypothesis is that there's an epigenetic effect on the Y chromosome,” says Costa. This effect is consistent with studies in remote Swedish villages, where shortages in food supply had a [generational effect down the male line](#), but not the female line.

But what if this increased risk of death was due to a legacy of the father's trauma that had nothing to do with DNA? What if traumatised fathers were more likely to abuse their children, leading to long-term

health consequences, and sons bore the brunt of it more than daughters?

## **Children born to men before they became PoWs didn't have a spike in mortality, but the sons of the same men after their PoW camp experience did**

Once again, comparing the health of children within families helped rule this out. Children born to men before they became PoWs didn't have a spike in mortality. But the sons of the same men after their PoW camp experience did.

"It's a case of ruling out the other possible options," says Costa. "A lot of it is proof by elimination and what is the most consistent explanation."

Many of the times when trauma is thought to have echoed down the generations via epigenetics in humans are linked to the darkest moments in history. Wars, [famines](#) and [genocides](#) are all thought to have left an epigenetic mark on the descendants of those who suffered them.



An epigenetic signal in the children of people who have survived traumatic experiences raises hopes of reversing the effect it has on their DNA (Credit: Alamy/Getty Images/BBC)

Some studies have proved more controversial than others. A 2015 study found that the children of the [survivors of the Holocaust had epigenetic changes](#) to a gene that was linked to their levels of cortisol, a hormone involved in the stress response.

"The idea of a signal, an epigenetic finding that is in offspring of trauma survivors can mean a lot of things," says Rachel Yehuda, director of the Traumatic Stress Studies Division at the Mount Sinai School of Medicine and an author of the study. "It's exciting that it's there."

The study was small, assessing just 32 Holocaust survivors and a total of 22 of their children, with a small control group. Researchers have [criticised the conclusions of the study](#). Without looking at several generations and searching more widely in the genome, we can't be sure it is really epigenetic inheritance.

Yehuda acknowledges that [the paper was blown out of proportion](#) in some reports, and larger studies assessing several generations would be needed draw firm conclusions.

“It was one single small study, a cross-section of adults many, many years after parental trauma. The fact we got a hint was big news,” says Yehuda. “Now the question is, how do you put meat on the bones? How do you really understand the mechanism of what is happening?”

## **When pups smelled the scent of cherry blossom, they became more jumpy and nervous than pups whose fathers hadn't been conditioned to fear it**

Controlled experiments in mice have allowed researchers to hone in on this question. A 2013 study found that there was an [intergenerational effect of trauma associated with scent](#). The researchers blew acetophenone – which has the scent of cherry blossom – through the cages of adult male mice, zapping their foot with an electric current at the same time. Over several repetitions, the mice associated the smell of cherry blossom with pain.



The idea that the effect of a traumatic experience might be passed from a parent to their offspring is still regarded as controversial by many (Credit: Alamy/Getty Images/BBC)

Shortly afterwards, these males bred with female mice. When their pups smelled the scent of cherry blossom, they became more jumpy and nervous than pups whose fathers hadn't been conditioned to fear

it. To rule out that the pups were somehow learning about the smell from their parents, they were raised by unrelated mice who had never smelt cherry blossom.

The grandpups of the traumatised males also showed heightened sensitivity to the scent. Neither of the generations showed a greater sensitivity to smells other than cherry blossom, indicating that the inheritance was specific to that scent.

This sensitivity to cherry blossom scent was linked back to epigenetic modifications in their sperm DNA. Chemical markers on their DNA were found on a gene encoding a smell receptor, expressed in the olfactory bulb between the nose and the brain, which is involved in sensing the cherry blossom scent. When the team dissected the pups' brains they also found there was a greater number of the neurons that detect the cherry blossom scent, compared with control mice.

## **It is not that fear is being passed down the generations – it is that fear in one generation leads to sensitivity in the next**

The second and third generation appeared to have not a fear of the scent itself, but a heightened sensitivity to it. The finding brings to light an often-missed subtlety of epigenetic inheritance – that the next generation doesn't always show exactly the same trait that their parents developed. It is not that fear is being passed down the generations – it is that fear of a scent in one generation leads to sensitivity to the same scent in the next.

“So this is not ‘apples for apples’,” says Brian Dias, author of the study and a researcher at Emory University and the Yerkes National Primate Research Center in the US. Even the term “inheritance” should be qualified here, he adds. “The word inheritance suggests it has to be a faithful representation of a trait that’s passed down.”

The consequences of passing down the effects of trauma are huge, even if they are subtly altered between generations. It would change the way we view how our lives in the context of our parents' experience, influencing our physiology and even our mental health.



The offspring of mice conditioned to fear the smell of flowers would also be sensitive to the same scent (Credit: Alamy/Getty Images/BBC)

And knowing that the consequences of our own actions and experiences now could affect the lives of our children – even long before they might be conceived – could put a very different spin on how we choose to live.

Despite picking up these echoes of trauma down the generations, there is a big stumbling block with research into epigenetic inheritance: no one is sure how it happens. Some scientists think that it is [actually a very rare event](#).

One of the reasons that it may not be widespread is that the vast majority of one type of epigenetic mark on the DNA – the addition of a clump of chemicals known as methylation – is wiped clean at the very start of life and the process of adding these chemical groups to the DNA begins almost from scratch.

## **Despite these echoes of trauma down the generations, there is a big stumbling block with research into epigenetic inheritance: no one is sure how it happens**

“As soon as the sperm enters the egg in a mammal, there’s a rapid loss of DNA methylation from the paternal set of chromosomes,” says Anne Ferguson-Smith, a researcher studying epigenetics at the University of Cambridge. “That’s the reason why transgenerational epigenetic inheritance is such a surprise.

“It’s very hard to imagine how you could have epigenetic inheritance when there’s a process of removal of all the epigenetic marks and putting on new ones in the next generation.”

There are, however, parts of the genome that are not wiped clean. A process called genomic imprinting protects the methylation at specific points of the genome. But these sites are not the ones where the epigenetic changes relevant to trauma are found.

A recent study by Ferguson-Smith's group [suggests epigenetic inheritance is probably very rare](#) in mice.



Epigenetics is thought to be the link between nature and nurture, where a person's experiences alters how their DNA is read by their cells (Credit: Alamy/Getty Images/BBC)

But other researchers are convinced that they have found the hallmarks of epigenetic inheritance for several traits – in humans as well as animals. What's more, they think they've found a mechanism for how it works. This time it could be molecules similar to DNA – known as RNA – that are altering how genes function.

A recent paper has revealed strong [evidence that RNA may play a role in how the effects of trauma can be inherited](#). Researchers examined how trauma early in life could be passed on by taking mouse pups away from their mothers right after birth.

“Our model is quite unique,” says [Isabelle Mansuy](#) of the University of Zürich and ETH Zürich, who led the research. “It’s to mimic dislocated families, or the abuse, neglect and emotional damage that you sometimes see in people.”

The symptoms these pups showed as they grew up also mimicked the symptoms seen in children who have experienced early trauma. The mice showed signs of increased risk-taking and higher calorie intake, both seen in child trauma survivors. When the males grew up, they had pups that showed similar traits – overeating, risk taking and higher levels of antisocial behaviour.

## The pups showed the typical altered behavioural patterns of those whose parents experienced trauma

The researchers extracted RNA molecules from the sperm of male mice who had been traumatised and injected these molecules into early the embryos of mice whose parents had not experienced this early-life trauma. The resulting pups, however, showed the typical altered behavioural patterns of a pup whose parents experienced trauma.

They also found that different lengths of RNA molecules were linked to different behavioural patterns: longer RNAs corresponded to greater food intake, changed the body's response to insulin and greater risk-taking. Smaller RNA molecules were linked to showing signs of despair.

“It's the first time we've seen this link in a causal way,” says Mansuy.



It is possible that emotional damage experienced in your own childhood could be passed on to your children (Credit: Alamy/Getty Images/BBC)

How these RNA molecules alter the behaviour of multiple generations is not yet known. Mansuy is now running experiments in humans to see if similar processes are at work in humans. Initial experiments by other researchers have shown that [this does seem to be the case in men](#).

This research – as well as many of the mice studies – focus on sperm and epigenetic inheritance down the male line. This isn't because scientists think it only happens in males. It's just a lot harder to study eggs than it is to study sperm.

But efforts to decipher epigenetic inheritance down the female line is the next step.

“We had to start from somewhere,” says Mansuy. “But we are looking to have a model of trauma that shows how inheritance occurs via both females and males.”

## **The science of epigenetic inheritance of the effects of trauma is young, which means it is still generating heated debate**

There are other known kinds of epigenetic mechanisms that are relatively little studied. One of them is called histone modification, where the proteins that act as a scaffold for DNA are chemically tagged. Now research is starting to suggest that [histones could also be involved in epigenetic inheritance](#) through the generations in mammals.

“I suspect the answer is that all of these mechanisms could interact to give us the phenomenon that is intergenerational inheritance of acquired traits,” says Dias.

The science of epigenetic inheritance of the effects of trauma is young, which means it is still generating heated debate. For Yehuda, who did pioneering work on Post-Traumatic Stress Disorder in the 1990s, this comes with a sense of déjà vu.



Exactly how trauma is passed down through the generations is still unclear as the mechanisms that act on the DNA are not fully understood (Credit: Alamy/Getty Images/BBC)

“Where we are with epigenetics today feels like how it was when we first started doing research into PTSD,” she says. “It was a controversial diagnosis. Not everyone believed there could be long term effect of trauma.”

Nearly 30 years later, PTSD is a medically accepted condition that explains why the legacy of trauma can span decades in a person’s lifetime.

But if trauma is shown to be passed down the generations in humans in the same way as it appears to be in mice, we shouldn't feel a sense of inevitability about this inheritance, says Dias.

Using his cherry blossom experiments in mice, he tested what would happen if males that feared the scent were later desensitised to the smell. The mice were repeatedly exposed to the scent without receiving a foot shock.

"The mouse hasn't forgotten, but a new association is being formed now this odour is no longer paired with the foot shock," says Dias.

When he looked at their sperm, they had [lost their characteristic "fearful" epigenetic signature](#) after the desensitisation process. The pups of these mice also no longer showed the heightened sensitivity to the scent. So, if a mouse "unlearns" the association of a scent and pain, then the next generation may escape the effects.

It also suggests that if humans inherit trauma in similar ways, the effect on our DNA could be undone using techniques like cognitive behavioural therapy.

"There's a malleability to the system," says Dias. "The die is not cast. For the most part, we are not messed up as a human race, even though trauma abounds in our environment."

At least in some cases, Dias says, healing the effects of trauma in our lifetimes can put a stop to it echoing further down the generations.

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*The artworks in this article were created by Javier Hirschfeld for the BBC.*