Life is like a pinball game – the chances of enjoying good health and prosperity are unevenly distrib-uted. Those who face difficult starting conditions struggle to achieve success and progress. Players with a good head start, on the other hand, achieve the top scores.

PHOTO: ADOBESTOCK

HIGH SCORE IN THE GAME OF LIFE

TEXT: MICHAELA HUTTERER

Genes, environment, society – these are factors we cannot freely choose, but that nonetheless shape us and interact with one another in remarkable ways. Traumatic experiences and life circumstances influence how our genes function. Laurel Raffington at the Max Planck Institute for Human Development in Berlin studies how genetic predispositions and early social disadvantage interact – and what can be done to mitigate the negative effects.

PHOTO: ARNE SATTLER FOR MPG

Developmental psychologist Laurel Raffington studies how social inequality and genetic predisposition influence the development of children and adolescents.

Two players stand by a unique pinball machine: "Genetic Pinball" is emblazoned above it. Both players are looking to beat the high score and rack up as many points as possible in the top areas of the gamescape: education, health, and status. Chance determines not only the size of the pinball – representing genetic disposition – but also where the ball enters the game. Player 1, in this round, comes from a wealthy family. His ball is large and starts close to the high-scoring areas like education and health. Player 2 has less favorable starting conditions: money is tight, even for schooling and healthcare. She starts on the opposite side of the playing field, and her ball is much smaller. While Player 1's ball collects points with ease, Player 2 requires great skill to get hers into the high-scoring areas. Far too often, her ball ends up out of play or falls into one of the holes on the playfield, where only the small balls can go. These holes represent life's challenges, like an inaccessible education system. Does Player 2 even have a chance of beating the high score?

What may feel unfair in the game is actually a reflection of real-world findings from a 2020 perspective review paper, brought to life as a video game by a creative agency. From May to October, visitors aboard the exhibition ship MS Wissenschaft were able to experience how genes and socioeconomic factors shape a person's life. Circumstances they couldn't control because they – like our genetic disposition – are determined by chance.

Understanding early childhood influences

"We have no control over the genes we're born with, the family we grow up in, or the country we're from," says developmental psychologist Laurel Raffington. "But our genes, our upbringing, the environment, our diet, and family stress – all of these factors affect our health later in life." Raffington leads the research group Biosocial at the Max Planck Institute for Human Development in Berlin. Together with her team, she examines how genetic influences and social inequality in childhood combine to shape differential outcomes of education and health across the lifespan.

For decades, the human genome was considered the definitive and unchangeable blueprint of life. Whether it's appearance, personality, or disease risk: all information is stored in our DNA as sequences of the bases adenine, guanine, cytosine, and thymine. Each of our roughly 250 different cell types has the same genetic sequence, but not all genes are active in every cell. The liver produces liver cells, and the skin forms skin cells. So, what determines which genes a cell uses? Biochemical processes silence certain genes, preventing them from being expressed. These epigenetic markers control which genes are active, and unlike DNA, they are remarkably flexible: a person's epigenetic profile responds to external influences, including harmful ones.

"We know that children from socially disadvantaged families are more often exposed to unfavorable living conditions, such as poorer diets, more exposure to air pollution, environmental toxins, and family stress," says Laurel Raffington. "This puts them at greater risk of lower educational achievement and a wide range of illnesses." But can this be detected in the epigenetic profiles of

SUMMARY

Human development occurs through a complex interplay of genetic traits, environmental factors, and societal structures.

The genetic predispositions that are activated depend on our life circumstances both before and after birth.

Epigenetics shows that our biological age is influenced by socioeconomic inequality (poverty) and nutrition.

“Human development unfolds in transactions between genes and social environments.”

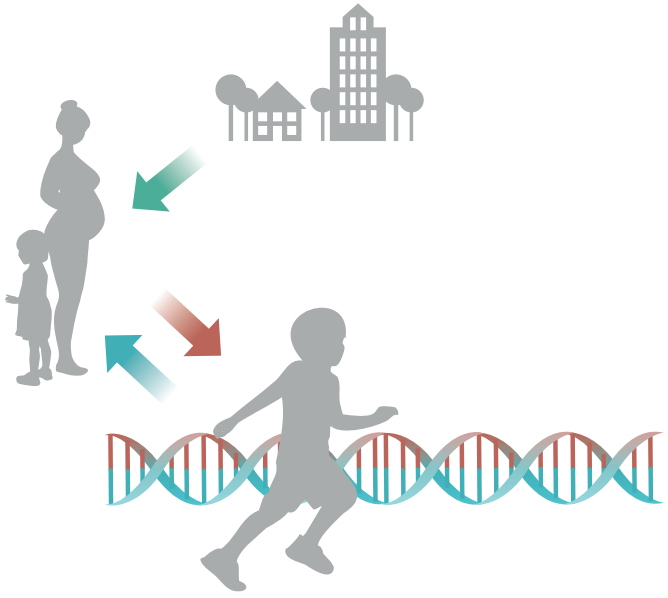
LAUREL RAFFINGTON

the affected children? After all, the effects of adverse childhood circumstances often do not become apparent until decades later.

Adopting an innovative approach to investigate this question, Laurel Raffington and her team analyzed saliva samples from over 3200 adolescents aged 8 to 18 in the United States. The researchers observed that children from socially disadvantaged backgrounds already showed epigenetic profiles that were linked in previous adult studies to poorer health outcomes, such as an increased risk of obesity and a higher biological age. “Previous studies have already shown that children growing up in financial poverty are more likely to suffer a higher disease burden later in life and to have a shorter life expectancy,” says Laurel Raffington. “We now believe we have identified measurements that can capture this ‘long arm’ of childhood in real time – and, with it, the long-term effects of environmental influences and developmental processes during childhood.”

It is not only physical experiences that shape us, but also psychological ones: in 2015, Elisabeth Binder, director at the Max Planck Institute of Psychiatry in Munich, discovered that childhood trauma experienced by mothers can later be passed down to their children. “We found epigenetic changes in a gene involved in stress regulation in the children,” reports the neuroscientist. The multiple severely negative experiences endured by 32 mothers during the Holocaust influenced the regulation of a gene in their children that controls the stress hormone system. Since the children did not share their mothers’ experiences, these must have been transmitted by the parents.

Experiences of violence and trauma also leave their mark on the epigenome. Elisabeth Binder studies how genetic predisposition and external factors interact to increase the risk of psychiatric disorders. “Negative life events have a strong impact on the risk of psychiatric disorders. And the risk is especially pronounced when these events occurred during childhood,” says Binder. One reason for this lies in brain development, which is not complete until the early 20s. Up until then, the brain is particularly receptive to external influences – both positive and negative.



GRAPHIC GCO BASED ON WORK BY THE MPI FOR HUMAN DEVELOPMENT

Interaction: life circumstances and genetic predisposition influence our health. Health, in turn, affects gene activity – starting in the womb and continuing throughout life.

It’s also known that the epigenetic imprints of trauma, nutritional status during pregnancy, environmental toxins, and smoking appear to be passed down across generations. Studies in transgenerational epigenetics in animals have shown this. How the process works in →

humans is still being studied. For example, children born during the Dutch Hunger Winter of 1944–1945 were more likely to develop obesity as adults. There is no purely genetic explanation for this.

Epigenetic research also reveals constructive insights: "Finding epigenetic differences in children doesn't necessarily mean their development is irreversibly determined," says Raffington. "Because epigenetic markers on genes are malleable, it may be possible to reverse health-damaging patterns and promote longevity. To what degree and at what age this is possible is not well understood." Epigenetic influences on health explain why not all people with the same genetic predisposition actually develop the disease. Studies on twins provide key insights here. "Twins, even identical ones, often die from different diseases despite having the same DNA. The probability of dying from coronary heart disease if you have an identical twin who has died from it is about 40 not 100 percent, and this figure varies by gender and age."

For Laurel Raffington, these observations demonstrate that the interaction between genes and the environment is a developmental process. "To some extent, we can likely still change the course set during youth," she says. She points to studies showing that epigenetic profiles of aging improve when people eat healthier or quit smoking. Smoking alters the epigenome of cells, causing genes to acquire disease-promoting traits. "When a person stops smoking or improves their nutrition in adulthood, epigenetic profiles of aging are decelerated.

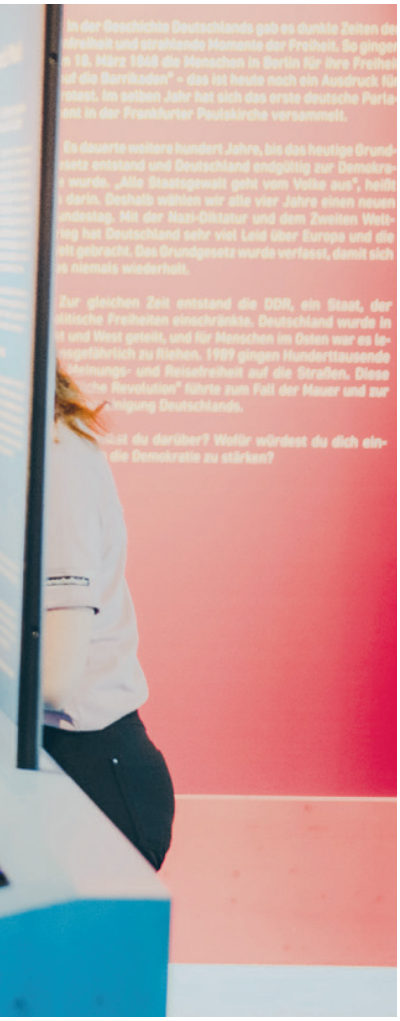
Young people on the exhibition ship MS Wissenschaft play the game Genetic Pinball to see how genetic predisposition and life circumstances shape their lives.

PHOTO: ILJA C. HENDEL, SCIENCE IN DIALOGUE

But those effects may be smaller in magnitude compared to health-promoting influences in utero and childhood," explains Raffington. The sooner life circumstances and lifestyle change, the lower the risk of activating a predisposition for age-related diseases.

Setting the course early

"Our research suggests that childhood poverty is correlated with children's epigenetic profiles of aging. This is consistent with a large literature linking childhood poverty to worse health later in life. What is new about our research is that our findings suggest we may be able to measure the long-term health impacts of childhood environments and development in real-time with this method of epigenetic profiling. We may not need to wait five decades to see what a policy intervention – like financial support – delivered to families and children does to their well-being in later life."



Laurel Raffington, Elisabeth Binder, and colleagues are now probing whether providing cash gifts to American mothers living near the poverty threshold affect their children's epigenetic profiles. In the Baby's First Years study, mothers received either USD 333 or 20 per month, starting at the birth of their child and continuing for six years. The US has no support benefits like Germany's child allowance, the only exception being a tax rebate for parents during the pandemic. By now, these children are almost six years old. Raffington is leading the investigation into whether the financial support not only changed the children's living conditions, but also affected their epigenetic profiles. "Previous results from my colleagues show that, during the first three years, high-cash gift households spent more money on child-specific goods and more time on early learning activities than the low-cash gift group. Mothers in the high-cash gift group also reported higher child consumption of fresh produce at age 2 years," says Raffington. Initial epigenetic findings are expected to be published by the Max Planck researchers in 2025.

Studies on the epigenetic impact on children don't just help us understand more about the gene-environment interaction that shapes us: they also offer political and social insights. "As individuals, we have no choice in selecting our genetic disposition or family," Raffington points out. "However, as a society, we have the freedom to address social inequality and optimize our education and healthcare systems to promote our own and the next generation's well-being."

Anyone who's interested can try out the genetic pinball machine for themselves to see how easy it is to change structures – at least in the game. Laurel Raffington and her team, in collaboration with game developer Purple Sloth, designed a second level where players can alter key parameters of the field and, for example, reduce social inequalities. On the MS Wissenschaft, players used Level 2 to improve access to education for children from non-academic households. That would be one fewer pinball trap for the less privileged ball.

www.mpg.de/podcasts/laurel-raffington (in German)

What determines success in life, and what can we choose freely? Simply scan the QR code and find out online.

GLOSSARY

EPIGENETICS
The term refers to a subfield of biology that focuses on cellular processes which influence gene activity.

EPIGENOME
This comprises all chemical changes to DNA and the proteins attached to it (such as histones) that regulate gene activity without altering the DNA sequence itself. These changes affect the function of the cells.

BIOLOGICAL AGE
This expresses the health and functional state of the body, measured by its actual health and performance. It can differ from the number of years lived.