

The medications that change who we are

 [bbc.com/future/article/20200108-the-medications-that-change-who-we-are](https://www.bbc.com/future/article/20200108-the-medications-that-change-who-we-are)

They've been linked to road rage, pathological gambling, and complicated acts of fraud. Some make us less neurotic, and others may even shape our social relationships. It turns out many ordinary medications don't just affect our bodies – they affect our brains. Why? And should there be warnings on packets?

“Patient Five” was in his late 50s when a trip to the doctors changed his life.

He had diabetes, and he had signed up for a study to see if taking a “statin” – a kind of cholesterol-lowering drug – might help. So far, so normal.

But soon after he began the treatment, his wife began to notice a sinister transformation. A previously reasonable man, he became explosively angry and – out of nowhere – developed a tendency for road rage. During one memorable episode, he warned his family to keep away, lest he put them in hospital.

Out of fear of what might happen, Patient Five stopped driving. Even as a passenger, his outbursts often forced his wife to abandon their journeys and turn back. Afterwards, she'd leave him alone to watch TV and calm down. She became increasingly fearful for her own safety.

Then one day, Patient Five had an epiphany. “He was like, ‘Wow, it really seems that these problems started when I enrolled in this study’,” says Beatrice Golomb, who leads a research group at the University of California, San Diego.

Alarmed, the couple turned to the study's organisers. “They were very hostile. They said that the two couldn't possibly be related, that he needed to keep taking the medication, and that he should stay in the study,” says Golomb.

Ironically, by this point the patient was so cantankerous that he flatly ignored the doctors' advice. “He swore roundly, stormed out of the office and stopped taking the drug immediately,” she says. Two weeks later, he had his personality back.

Others have not been so lucky. Over the years, Golomb has collected reports from patients across the United States – tales of broken marriages, destroyed careers, and a surprising number of men who have come unnervingly close to murdering their

wives. In almost every case, the symptoms began when they started taking statins, then promptly returned to normal when they stopped; one man repeated this cycle five times before he realised what was going on.

Antidepressants may not just lighten moods, they may also reduce expressions of neuroticism, research suggests (Credit: Getty Images)

According to Golomb, this is typical – in her experience, most patients struggle to recognise their own behavioural changes, let alone connect them to their medication. In some instances, the realisation comes too late: the researcher was contacted by the families of a number of people, including an internationally renowned scientist and a former editor of a legal publication, who took their own lives.

We're all familiar with the mind-bending properties of psychedelic drugs – but it turns out ordinary medications can be just as potent. From paracetamol (known as acetaminophen in the US) to antihistamines, statins, asthma medications and antidepressants, there's emerging evidence that they can make us impulsive, angry, or restless, diminish our empathy for strangers, and even manipulate fundamental aspects of our personalities, such as how neurotic we are.

In most people, these changes are extremely subtle. But in some they can also be dramatic.

The list of potential culprits includes some of the most widely consumed drugs on the planet

Back in 2011, a French father-of-two sued the pharmaceutical company GlaxoSmithKline, claiming that the drug he was taking for Parkinson's disease had turned him into a gambler and gay sex addict, and was responsible for risky behaviours that had led to him being raped.

Then in 2015, a man who targeted young girls on the internet used the argument that the anti-obesity drug Duromine made him do it – he said that it reduced his ability to control his impulses. Every now and again, murderers try to blame sedatives or antidepressants for their offences.

If these claims are true, the implications are profound. The list of potential culprits includes some of the most widely consumed drugs on the planet, meaning that even if the effects are small at an individual level, they could be shaping the personalities of millions of people.

Research into these effects couldn't come at a better time. The world is in the midst of a crisis of over-medication, with the US alone buying up 49,000 tonnes of paracetamol every year – equivalent to about 298 paracetamol tablets per person – and the average American consuming \$1,200 worth of prescription medications over the same period. And as the global population ages, our drug-lust is set to spiral even further out of control; in the UK, one in 10 people over the age of 65 already takes eight medications every week.

In the US, more than 49,000 tons of paracetamol is consumed every year - the equivalent of 298 pills per person (Credit: Getty Images)

How are all these medications affecting our brains? And should there be warnings on packets?

Golomb first suspected a connection between statins and personality changes nearly two decades ago, after a series of mysterious discoveries, such as that people with lower cholesterol levels are more likely to die violent deaths. Then one day, she was chatting to a cholesterol expert about the potential link in the hallway at her work, when he brushed it off as obviously nonsense. “And I said ‘how do we know that?’,” she says.

Filled with fresh determination, Golomb scoured the scientific and medical literature for clues. “There was shockingly more evidence than I had imagined,” she says. For one thing, she uncovered findings that if you put primates on a low-cholesterol diet, they become more aggressive.

Golomb remains convinced that lower cholesterol can cause behavioural changes in both men and women

There was even a potential mechanism: lowering the animals' cholesterol seemed to affect their levels of serotonin, an important brain chemical thought to be involved in regulating mood and social behaviour in animals. Even fruit flies start fighting if you mess up their serotonin levels, but it also has some unpleasant effects in people – studies have linked it to violence, impulsivity, suicide and murder.

If statins were affecting people's brains, this was likely to be a direct consequence of their ability to lower cholesterol.

Since then, more direct evidence has emerged. Several studies have supported a potential link between irritability and statins, including a randomised controlled trial – the gold-standard of scientific research – that Golomb led, involving more than 1,000 people. It found that the drug increased aggression in post-menopausal women though, oddly, not in men.

In 2018, a study uncovered the same effect in fish. Giving statins to Nile tilapia made them more confrontational and – crucially – altered the levels of serotonin in their brains. This suggests that the mechanism that links cholesterol and violence may have been around for millions of years.

Golomb remains convinced that lower cholesterol, and, by extension, statins, can cause behavioural changes in both men and women, though the strength of the effect varies drastically from person to person. “There are lines of evidence converging,” she says, citing a study she conducted in Sweden, which involved comparing a database of the cholesterol levels of 250,000 people with local crime records. “Even adjusting for confounding factors, it was still the case that people with lower cholesterol at baseline were significantly more likely to be arrested for violent crimes.”.



Fruit flies become more aggressive when their serotonin levels become mixed up, research has shown (Credit: Getty Images)

But Golomb's most unsettling discovery isn't so much the impact that ordinary drugs can have on who we are – it's the lack of interest in uncovering it. "There's much more of an emphasis on things that doctors can easily measure," she says, explaining that, for a long time, research into the side-effects of statins was all focused on the muscles and liver, because any problems in these organs can be detected using standard blood tests.

This is something that Dominik Mischkowski, a pain researcher from Ohio University, has also noticed. "There is a remarkable gap in the research actually, when it comes to the effects of medication on personality and behaviour," he says. "We know a lot about the physiological effects of these drugs – whether they have physical side effects or not, you know. But we don't understand how they influence human behaviour."

Mischkowski's own research has uncovered a sinister side-effect of paracetamol. For a long time, scientists have known that the drug blunts physical pain by reducing activity in certain brain areas, such as the insular cortex, which plays an important role in our emotions. These areas are involved in our experience of social pain, too – and intriguingly, paracetamol can make us feel better after a rejection.

Mischkowski wondered whether painkillers might be making it harder to experience empathy

And recent research has revealed that this patch of cerebral real-estate is more crowded than anyone previously thought, because it turns out the brain's pain centres also share their home with empathy.

For example, fMRI (functional magnetic resonance imaging) scans have shown that the same areas of our brain become active when we're experiencing "positive empathy" –pleasure on other people's behalf – as when we're experiencing pain.

Given these facts, Mischkowski wondered whether painkillers might be making it harder to experience empathy. Earlier this year, together with colleagues from Ohio University and Ohio State University, he recruited some students and spilt them into two groups. One received a standard 1,000mg dose of paracetamol, while the other was given a placebo. Then he asked them to read scenarios about uplifting experiences that had happened to other people, such as the good fortune of "Alex", who finally plucked up the courage to ask a girl on a date (she said yes).



L-dopa is the most successful treatment for Parkinson's, but it can have side effects, making people act more impulsively (Credit: Getty Images)

The results revealed that paracetamol significantly reduces our ability to feel positive empathy – a result with implications for how the drug is shaping the social relationships of millions of people every day. Though the experiment didn't look at negative empathy – where we experience and relate to other people's pain – Mischkowski suspects that this would also be more difficult to summon after taking the drug.

“I'm not entirely junior anymore as a researcher, and to be honest, this line of research is really the most worrisome that I've ever conducted,” he says. “Especially because I'm well aware of the numbers [of people] involved. When you give somebody a drug, you don't just give it to a person – you give it to a social system. And we really don't understand the effects of these medications in the broader context.”

Empathy doesn't just determine if you're a “nice” person, or if you cry while you're watching sad movies. The emotion comes with many practical benefits, including more stable romantic relationships, better-adjusted children, and more successful careers – some scientists have even suggested that it's responsible for the triumph of our species. In fact, a quick glance at its many benefits reveals that casually lowering a person's ability to empathise is no trivial matter.

Scientists have known for a while that the medications used to treat asthma are sometimes associated with behavioural changes, such as an increase in hyperactivity

Technically, paracetamol isn't changing our personalities, because the effects only last a few hours and few of us take it continuously. But Mischkowski stresses that we do need to be informed about the ways it affects us, so that we can use our common sense. "Just like we should be aware that you shouldn't get in front of the wheel if you're under the influence of alcohol, you don't want to take paracetamol and then put yourself into a situation that requires you to be emotionally responsive – like having a serious conversation with a partner or co-worker."

One reason medications can have such psychological clout is that the body isn't just a bag of separate organs, awash with chemicals with well-defined roles – instead, it's a network, in which many different processes are linked.

For example, scientists have known for a while that the medications used to treat asthma are sometimes associated with behavioural changes, such as an increase in hyperactivity and the development of ADHD symptoms. Then, more recently, research uncovered a mysterious connection between the two disorders themselves; having one increases the risk of having the other by 45-53%. No one knows why, but one idea is that asthma medications bring on ADHD symptoms by altering levels of serotonin or inflammatory chemicals, which are thought to be involved in the development of both conditions.



There have been many reports of severe psychological change from the use of statins (Credit: Getty Images)

Sometimes these links are more obvious. Back in 2009, a team of psychologists from Northwestern University, Illinois, decided to check if antidepressants might be affecting our personalities. In particular, the team were interested in neuroticism. This “Big Five” personality trait is epitomised by anxious feelings, such as fear, jealousy, envy and guilt.

For the study, the team recruited adults who had moderate to severe depression. They gave one third of the study’s participants the antidepressant paroxetine (a kind of selective serotonin reuptake inhibitor (SSRI)), one third a placebo, and one third talking therapy. They then checked to see how their mood and personalities changed from the beginning to the end of a 16-week treatment.

“We found that massive changes in neuroticism were brought about by the medicine and not very much at all by the placebo [or the therapy],” says Robert DeRubeis, who was involved in the study. “It was quite striking.”

The idea that antidepressants are affecting neuroticism directly is intriguing

The big surprise was that, though the antidepressants did make the participants feel less depressed, the reduction in neuroticism was much more powerful – and their influence on neuroticism was independent of their impact on depression. The patients on antidepressants also started to score more highly for extroversion.

It's important to note that it was a relatively small study, and no one has tried to repeat the results yet, so they may not be totally reliable. But the idea that antidepressants are affecting neuroticism directly is intriguing. One idea is that the trait is linked to level of serotonin in the brain, which is altered by the SSRIs.

While becoming less neurotic might sound like an appealing side-effect, it's not necessarily all good news. That's because this aspect of our personalities is something of a double-edged sword; yes, it's been associated with all kinds of unpleasant outcomes, such as an earlier death, but it's also thought that anxious over-thinking might be helpful. For example, neurotic individuals tend to be more risk-averse, and in certain situations worrying can improve a person's performance.



Cholesterol-lowering drugs save tens of thousands of lives every year, so people should seek medical advice before stopping taking them (Credit: Getty Images)

“What [the American psychiatrist] Peter Kramer warned us about was that when some people are on antidepressants, what can happen is that they begin not to care about things that people care about,” says DeRubeis. If the results do hold up, should patients be warned about how their treatment might change them?

“If I were advising a friend, I would certainly want them to be on the lookout for those kinds of undesirable effects, just like they would naturally be looking out for other side-effects, like whether they're gaining weight, and so on,” says DeRubeis.

At this point it's worth pointing out that no one is arguing that people should stop taking their medication. Despite their subtle effects on the brain, antidepressants have been shown to help prevent suicides, cholesterol-lowering drugs save tens of thousands of lives every year, and paracetamol is on the World Health Organisation's list of essential drugs because of its ability to relieve pain. But it is important that people are informed about any potential psychological side-effects.

The association with impulsive behaviours makes sense, because L-dopa is essentially providing the brain with a dose of extra dopamine

The matter takes on a whole new urgency, when you consider that some personality changes can be dramatic. There's solid evidence that the drug L-dopa, which is used to treat Parkinson's disease, increases the risk of Impulse Control Disorders (ICDs) – a group of problems that make it more difficult to resist temptations and urges.

Consequently, the drug can have life-ruining consequences, as some patients suddenly start taking more risks, becoming pathological gamblers, excessive shoppers, and sex pests. In 2009, a drug with similar properties hit the headlines, after a man with Parkinson's committed a £45,000 (\$60,000) ticket scam. He blamed it on his medication, claiming that it had completely changed his personality.

The association with impulsive behaviours makes sense, because L-dopa is essentially providing the brain with a dose of extra dopamine – in Parkinson's disease the part of the brain that produces it is progressively destroyed – and the hormone is involved in providing us with feelings of pleasure and reward.

Experts agree that L-dopa is the most effective treatment for many of the symptoms of Parkinson's disease, and it's prescribed to thousands of people in the US every year. This is despite a long list of possible side effects that accompanies the medication, which explicitly mentions the risk of unusually strong urges, such as for gambling or sex.

In fact, DeRubeis, Golomb and Mischkowski are all of the opinion that the drugs they're studying will continue to be used, regardless of their potential psychological side-effects. "We are human beings, you know," says Mischkowski. "We take a lot of

stuff that is not necessarily always good in every circumstance. I always use the example of alcohol, because it's also a painkiller, like paracetamol. We take it because we feel that it has a benefit for us, and it's OK as long as you take it in the right circumstances and you don't consume too much."

But in order to minimise any undesirable effects and get the most out of the staggering quantities of medications that we all take each day, Mischkowski reiterates that we need to know more. Because at the moment, he says, how they are affecting the behaviour of individuals – and even entire societies – is largely a mystery.

--

Disclaimer

All content within this column is provided for general information only, and should not be treated as a substitute for the medical advice of your own doctor or any other health care professional. The BBC is not responsible or liable for any diagnosis made by a user based on the content of this site. The BBC is not liable for the contents of any external internet sites listed, nor does it endorse any commercial product or service mentioned or advised on any of the sites. Always consult your own GP if you're in any way concerned about your health.

*If you liked this story, **sign up for the weekly [bbc.com features newsletter](#)**, called "The Essential List". A handpicked selection of stories from BBC Future, Culture, Worklife, and Travel, delivered to your inbox every Friday.*