Rejection and heartbreak can have effects every bit as physical as cuts and bruises, and understanding why could change your life

IT STRUCK suddenly. First there was an ache in my chest, as if my sternum was laced too tightly. Then came the headaches and chronic tiredness. The feelings lingered for weeks, and were often at their worst just before I fell asleep each night. Though it was more than a decade ago, I remember it well, as it marked my first bout of an ailment that would be unmistakable forever after: heartbreak.

Betrayal, rejection and lost love are a fact of life, but it is only in the past 10 years that we have begun to unravel the basis of these hurt feelings in the brain. Scientists have found that the sting of rejection fires up the same neural pathways as the pain from a burn or bruise. Besides explaining why some people have thicker skins than others, this fact reveals an intimate link between your social life and your health - you really can die of loneliness.

Our language has long borrowed physical terms to describe our darkest emotions, with phrases such as "she broke my heart", "he burned me", and "he stabbed me in the back". Such comparisons occur around the world: Germans talk about being emotionally "wounded", while Tibetans describe rejection as a "hit in the heart".

Although these expressions were always taken to be metaphorical, there had been some early hints that more was afoot. Animal studies in the 1990s, for instance, showed that morphine not only relieves pain after injury, but can also reduce the grief of rat pups separated from their mother.

Still, when Naomi Eisenberger at the University of California, Los Angeles, started studying hurt feelings in humans in the early 2000s, she did not know what she would find. She was intrigued by the way that past rejections linger with us throughout life; we can all remember a time when we weren't picked for the school sports team or felt excluded by a group of friends. "I was curious - why is it such a big deal?" she says.

To find out what the brain is up to when people feel social rejection, Eisenberger asked volunteers...
to play a simple computer game called Cyberball, in which three players pass a ball among
themselves. Each volunteer was led to believe they were playing with two people who were in
another room, but in fact the playmates were controlled by the computer.

**Try Cyberball for yourself:** "CyberBall makes a game out of ostracism"

Although they started out friendly, the computerised players soon stopped throwing the ball to the
volunteer. It might seem like a trifling insult, but some subjects responded strongly to the slight -
slumping in their seats or making a rude hand gesture at the screen.

All the while, a functional MRI scanner recorded the volunteer's brain activity, revealing a surge in
the dorsal anterior cingulate cortex (dACC) when they began to feel isolated (Science, vol 302, p
290). This region is known to be an important part of the brain's "pain network", determining how
upsetting we find an injury. The response can vary depending on the situation; bumping your head
might seem like a big deal in the office, but during a football game you might barely notice the
blow.

Crucially, the more distressing you find an injury, the more the dACC lights up, a fact that also
seemed to play out during the games of Cyberball: those who reported feeling worst after the
rejection showed the greatest activity in this region.

Other studies confirmed the link, finding that social rejection provokes not just the dACC but also
the anterior insula, another part of the pain network that responds to our distress at a cut finger or
broken bone. But although these results all suggest that our anguish after an insult is the same as
our emotional response to an injury, it took until last year to show how those feelings might spill
over into tangible bodily sensations.

Ethan Kross at the University of Michigan in Ann Arbor decided to set Cyberball aside in favour of
a more serious form of rejection - a broken heart. He recruited 40 people who had been through a
break-up within the past six months and asked them to view a photo of their ex while reclining in
an fMRI scanner. He also instructed them to think in detail about the break-up. After a brief
intermission, the volunteers' forearms were given a painful jolt of heat, allowing Kross to compare
brain activity associated with the two situations.

As expected, the dACC and the anterior insula lit up in both cases. But surprisingly, the brain's
sensory centres, which reflect the physical discomfort that accompanies a wound, also showed
pronounced activity - the first evidence that the feeling of heartbreak can literally hurt (PNAS, vol
108, p 6270).

Cementing the connection between physical pain and emotional anguish, further studies have
found that the two experiences sometimes feed off one another. When people feel excluded, they
are more sensitive to the burn of a hot probe, and submerging a hand in ice water for 1 minute
leads people to report feeling ignored and isolated.

**Numbing the hurt**

The converse is also true: soothing the body's response to pain can alleviate the sting of an insult.
Nathan DeWall of the University of Kentucky, Lexington, recruited 62 students who either dosed
themselves up on two paracetamol (acetaminophen) pills every day for three weeks, or took a
placebo. Each evening, the students completed a questionnaire measuring their feelings of
rejection during the day. By the end of the three weeks, the group on paracetamol had developed
significantly thicker skins, reporting fewer hurt feelings during their day-to-day encounters. A
subsequent game of Cyberball confirmed the effect: those given paracetamol showed significantly
less activity in the dACC and the anterior insula compared to those taking the placebo
(Psychological Science, vol 21, p 931).
"The idea that you can actually affect people's experience socially with what is seen as such a mild, common drug [as paracetamol], that was a rather important validation," says Geoff MacDonald at the University of Toronto, Canada, one of the authors of the study. "This is exactly the kind of thing you would expect if this social pain thing is really true." Needless to say, due to the harmful side-effects of pain-killing drugs, you should not try this for yourself.

The work might explain why certain people find it harder to withstand the rough and tumble of their social lives than others. Extroverts have been shown to have a higher pain tolerance than introverts, and this is mirrored by their greater tolerance for social rejection. Eisenberger, meanwhile, has found that people who feel more pain when a hot electrode touches their arm are also more sensitive to hurt feelings during Cyberball.

These diverse reactions may be partly genetic. Eisenberger's team has shown that people with a small mutation to the gene OPRM1, which codes for one of the body's opioid receptors, are more likely to slip into depressed feelings after rejection than are those without the mutation. This same mutation also makes people more sensitive to physical pain, and they typically need more morphine following surgery.

Importantly, these receptors are particularly dense in the dACC. As you might expect, in people with the mutation, the dACC tends to react more strongly to perceived insults (PNAS, vol 106, p 15079).

As with many traits, a child's early environment can also determine their sensitivity. For instance, people with some forms of chronic pain are more likely to have had traumatic experiences, such as emotional abuse, during their early years. Perhaps it puts their pain network into overdrive, making them more sensitive to any discomfort (American Journal of Psychiatry, vol 162, p 899).

Adolescents seem particularly sensitive to rejection. The brain's pain network is still developing at their age and, compared to the adult brain, it tends to show a more exaggerated response to small slights and insults. On the positive side, social support during this period can carry lasting benefits. For instance, young adults who enjoyed tighter social networks in their late teens show more muted reactions to the sting of rejection than those who had felt lonelier in the past, perhaps because memories of past acceptance subconsciously sooth their feelings (Social Cognitive Affective Neuroscience, vol 7, p 106).

When you consider our ancestors' dependence on their social connections for survival, it makes sense for us to have evolved to feel rejection so keenly. Being kicked out of a tribe would have been akin to a death sentence, exposing our predecessors to starvation and predation. As a result, we needed a warning system that alerts us to a potential spat, preventing us from causing further offence and teaching us to toe the line in the future. The pain network, able to give us a jolt when we face physical injury from a fire or knife edge, would have been ideally equipped to curb our social behaviour.

Some have taken this line of thinking further, suggesting it might hold the secret to some of the more mysterious symptoms of loneliness. People who are lonely tend to have an increase in the expression of genes for inflammation, particularly in immune cells, and a decrease in the expression of antiviral genes.

Why would the body deal with isolation in this way? "That was kind of a puzzle to us for the last five or 10 years," says Steve Cole, a behavioural geneticist at the University of California, Los Angeles. An answer began to emerge when he looked at the way different conditions affect people with different social lives. Viruses spread quickly among large groups of people, whereas life-threatening bacterial infections generally come from wounds which our ancestors may have been more likely to receive when alone, without the protection of their peers. As a result, Cole suggests, our immune system may be "listening in" on our brain's signals of social status. If it looks as if we are enjoying a lively social life in a big group, we are geared up to deal with viruses;
if we feel alone, the dACC and other regions tune up inflammation, which helps us battle bacterial infection.

One piece of evidence for the idea comes from George Slavich, also at UCLA. He has found that socially stressful tasks, such as delivering an impromptu speech, trigger heightened activity in the dACC, prompting an inflammatory immune response - as if the brain were pre-empting the threat of isolation and injury (PNAS, vol 107, p 14817).

That response would have saved our ancestors from infection in the tooth-and-claw struggles of evolution, but it could backfire in the modern world. Increased inflammation has been linked to a host of conditions, including heart disease, cancer and Alzheimer's disease - and lonely people are at a greater risk of all of these. A meta-analysis in 2010 of 148 studies determined that people with adequate social connections were 1.5 times as likely to live to the end of the study period as lonely people - an effect on par with abstaining from smoking or excessive drinking (PLoS Medicine, vol 7, p e1000316). Another study, published this year, tracked the health of 2000 middle-aged and elderly US citizens. It found that those reporting the greatest feelings of loneliness were nearly twice as likely to die during the six-year study as those with the lowest levels of loneliness (Social Science and Medicine, vol 74, p 907).

The work would seem to emphasise the importance of social support programmes for the elderly and infirm, and anyone recovering from illness. Even so, much more research will be needed to understand the way our social lives influence our health, says John Cacioppo of the University of Chicago, who studies loneliness. He is sceptical that the Cyberball experiments tell us much about the impact of long-term isolation, pointing out that the known physiological responses to rejection are short-lived. "Loneliness may not be affected at all by those transient events," Cacioppo says. "The little things are not the things that are killing people - it's the brain being on alert in an unrelenting way."

In the meantime, there are measures we can take to smooth the bumpy road of our social lives. We all like to be comforted after an upset, but Eisenberger has found that giving support to others also softens our own response to rejection. To test this, she gave a man an electric shock while his female partner, lying in an fMRI scanner, could either hold his hand in support or was prohibited from doing so. When the woman could support her partner, her brain's response to threat and rejection was significantly subdued. Eisenberger plans to switch the gender roles in future work.

So although we can't stop life's situations from immediately shaping our emotional landscape, perhaps we do have a say in the way we respond to those events. Words may be as painful as sticks and stones, but by caring for others as well as ourselves, we can at least make sure that they hurt us only briefly.

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