

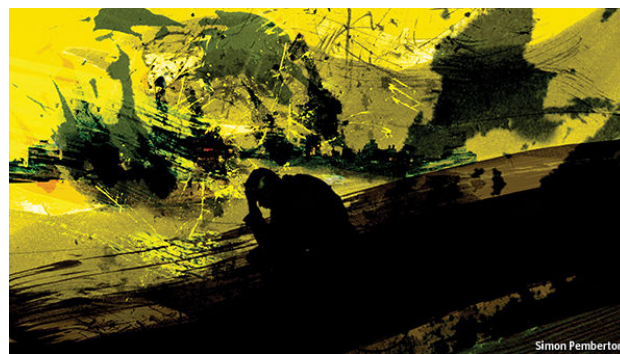
Post-traumatic stress disorder

Fear itself

A mental illness caused by trauma may be one of the first to be understood in physical terms

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ONE night in 2009 Jennifer Hopper and her fiancée, Teresa Butz, woke to find a man standing over them with a knife in his hand. He raped them both and killed Ms Butz with a stab through the heart. Ms Hopper was left with scars from slash wounds to her throat and arms. Her mental wounds healed more slowly. She became petrified of the dark and her sleep was disturbed by nightmares of intruders. A tap on the shoulder left her terrified. She could not get into her car: during the attack her worst fear had been that their assailant would drive them somewhere they would never be found.



Accounts of debilitating fear after trauma date back to the Trojan wars. In the 19th century survivors of train crashes were diagnosed with “railway spine” because doctors thought their hysteria was caused by compression of the backbone. In the first world war it was known as shell shock, soldier’s heart or battle fatigue. Not until soldiers returned from the Vietnam war with the same symptoms of hyper-vigilance, flashbacks and nightmares was the disorder truly taken seriously. In 1980 an umbrella term was coined: post-traumatic stress disorder (PTSD).

Attitudes are now quite different from those that prevailed during the second world war, when George Patton, an American general, threatened to court-martial men with battle fatigue. And research is progressing swiftly. A remarkable amount has been discovered about the causes of PTSD and how to treat it—which is welcome, because another discovery is how common it is.

War is the emblematic cause of PTSD. A recent study found that a quarter of American Vietnam veterans have had it and a tenth of those still alive continue to have severe symptoms. Last year a study among Syrian refugees in Turkey estimated that one in three had PTSD. Yet it is also widespread among people who live in poor, violent neighbourhoods: a study of inner-city

Atlanta found rates higher than among veterans.

A disorder's deep roots

PTSD is more common after repeated traumas than after a one-off; it is also more likely to emerge if the perpetrator is known to the victim. Trauma in early childhood, when the brain is still learning about the world and what should be feared, makes people more vulnerable in later life. So children abused by family members are at high risk of developing PTSD. Women are twice as likely as men to suffer, partly because domestic violence is a common cause of repeated trauma and because women are at much greater risk of sexual assault, which is particularly likely to cause PTSD.

What happens after a traumatic event influences people's chances of developing the disorder, including whether others are supportive or sceptical. Social and economic circumstances matter, too. Among Vietnam war veterans, school dropouts were more likely to develop it, even when levels of combat exposure were accounted for. But Matthew Friedman of America's National Centre for PTSD says some situations will overwhelm even those who have not a single risk factor. "It's a bit like George Orwell's Room 101 in '1984'," he says. "Everyone has a breaking point."

Sufferers are at much higher risk of developing other health problems, including diabetes, heart ailments, depression and addiction. They are also much more likely to be out of work, have marital problems or become teenage parents. As with other mental illnesses, they often have to bear the additional grief of their condition being dismissed as a character failing or at least less real than a physical illness.

But PTSD differs in one crucial respect from most other mental disorders: it can be modelled in other mammals, since they feel and show fear in much the same way humans do. Terrifying a mouse with an electric shock is simple; giving it a negative self-image is harder. Whereas many mood disorders are still mysterious, PTSD is increasingly well understood. According to Charles Marmar, a psychiatrist at New York University's medical centre, it may be the first psychiatric disorder "where we crack the mind-brain connections".

Neural research is helping to reveal how people get stuck in a state of fear. The amygdalae, a pair of almond-sized regions deep in the brain, are the main orchestrators of fear, reading incoming signals such as smells and sounds and sending messages to other bits of the brain, which filter the signals before reacting. In someone with PTSD the filters struggle to distinguish between real threats and those that can safely be ignored.

The brain of a healthy person given cause to panic will tell the body to activate various reactions,

including releasing adrenalin. A person's heart rate will increase and they will have a strong urge to fight or flee. Once back to safety, symptoms subside and all that remains is a bad memory. A woman assaulted in a noisy bar may react fearfully to the sound of clinking glasses for a few weeks, but over time, in what is called "fear extinction", the positive association of celebrating with friends will outweigh negative ones. The more often people receive such reminders without suffering a disaster, the more likely the fear is to dissipate—which is why it is important not to hide away after a trauma.

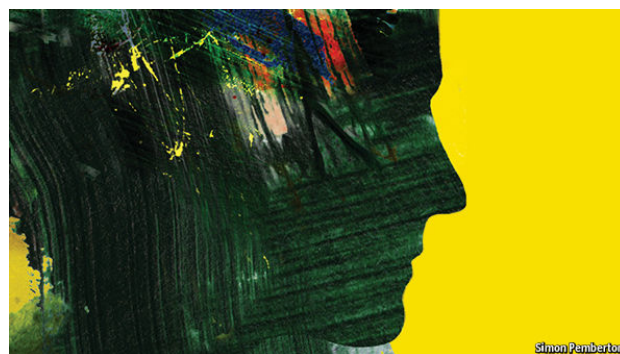
Retraining the brain

When this mechanism fails, the result is PTSD. A soldier returning from war may continue to freeze and have debilitating flashbacks when anything reminds him of combat. One ex-soldier tells of "freaking out" every time his wife baked: it turned out that the smell of almonds evoked Semtex, an explosive. People who were abused as children may suffer when it is dark, because such abuse often happens at night.

Studies of twins suggest that susceptibility to PTSD is about 30% genetic. Researchers in the new field of epigenetics—the study of how external factors influence the way the instructions written in genes are expressed in organisms—have produced some evidence to suggest that stress might be passed on to offspring.

An exciting recent development is the discovery of markers that show differences between the brains, genes and even blood of people with and without PTSD. When a sufferer sees a picture of a frightened face, the amygdala shows a heightened response. At the same time the prefrontal cortex, which regulates fear, is suppressed. Researchers are hot on the trail of chemicals that could indicate PTSD in a blood test, says Kerry Ressler, a molecular scientist and psychiatrist at McLean Hospital of Harvard Medical School.

Treatments mostly aim to retrain the brain's fear response. Many patients are given cognitive therapy, which teaches them to think differently about what happened and trains them to cope with triggers. Debra Kaysen of the University of Washington says severe symptoms recede in about four out of five patients following a dozen or so sessions. Other patients are given exposure therapy, in which they are confronted with the feared stimuli. Adults may be asked to describe a traumatic event in excruciating detail until it loses its potency; young children might play out what happened with toys. Virtual-reality simulations have been used on soldiers. One therapist compares the work to treating a burn victim: layer after layer.



Soon after her ordeal, Ms Hopper started cognitive therapy. The first aim was to get her back in her car. Her counsellor taught her to walk to it and replace intrusive thoughts (there could be someone hidden inside) with safe ones (I have parked here for years without problems). On around the tenth attempt, she managed to get back in. Conquering her fear of the dark took much longer, but eventually “one day my brain and body just caught up with my mind,” she says.

Most research on PTSD has focused on victims in rich countries, particularly America. But trauma happens everywhere. Dr Kaysen has adapted therapies developed in rich countries to survivors of torture in Iraq and rape in Congo. The results suggest that the disorder has the same characteristics in different locations and cultures, and also that similar treatments work—even in tough settings such as refugee camps.

New treatments are now being developed through animal experiments. One trial taught rats to fear a scent by spraying it at the same time as administering an electric shock; if it was sprayed repeatedly soon afterwards without a shock being administered, PTSD symptoms such as uncontrolled fear, measured by the animal’s “freezing” or heart-rate response, did not develop. Researchers then sought to find out whether there is a similar window of opportunity in humans who have experienced trauma. In a pilot programme in 2010, some patients who came into the emergency room at Grady Memorial Hospital in Atlanta following a rape, gunshot wound or car crash were given “imaginal exposure therapy”, in which they were asked to recall vividly what happened. Three months later, only half as many developed PTSD as in a comparable group that did not receive such therapy. Further trials will be needed to confirm that such early debriefings can help.

Recently Dr Ressler immobilised mice for two hours. They became more likely to develop PTSD-like symptoms after future trauma. Autopsies of their brains showed a change in gene expression that the researchers think might have caused the vulnerability. In a follow-up trial an experimental drug was used to target this gene and block the formation of fearful memories. Encouragingly, mice that had previously gone through the ordeal and then received the drug did not develop symptoms of PTSD when exposed to another frightening situation.

Amit Etkin and colleagues at Stanford University are studying how the brain circuits that control fear can be tweaked with the aid of SSRIs (a class of drugs, some of which are used to treat depression or anxiety) and transcranial magnetic stimulation, in which an electromagnet held close to the scalp transmits magnetic pulses to the brain. They found that stimulating a part of the frontal lobe can reduce activity in the amygdalae, which could lessen the symptoms of PTSD. Within five years, thinks Dr Etkin, new therapies will be available, including applying brain stimulation or using drugs to enhance the effects of talk therapy. Better treatments for other anxiety disorders, which afflict a third of Americans, could follow.

Even if new treatments for PTSD take longer to develop than hoped, acceptance of PTSD's inherently physical nature could encourage sufferers to seek help earlier. Rape victims in Dr Kaysen's practice typically waited 20 years before turning to her; Dr Marmar has treated veterans of the second world war who had tried to cope with their nightmares for as long as 40 years.

In a freezer in Boston are 50 samples of brain tissue donated to the world's first brain bank dedicated to the study of PTSD, set up by the Department of Veterans Affairs. More veterans and civilians, with and without the disorder, are filling in health questionnaires and pledging to donate brain tissue after death. Those who could not be healed themselves might help arm future generations against the same suffering, or perhaps, one day, help prevent it altogether.

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