

COVER



THE HIDDEN DAMAGE OF RAPE



Sexual violence causes psychological distress and results in inflammation that can accelerate ageing

Ricardo Zorzetto | ILLUSTRATIONS Catarina Bessell

In the time it takes you to read this article, another woman or girl will have been raped in Brazil. According to the “Violence against women in 2021” survey presented by the Brazilian Public Security Forum last March, the country recorded 56,098 cases of rape in 2021. This represents one rape every 9.4 minutes, or 153 a day. Three of every four victims are children aged under 14. These statistics, provided by the police and public security agencies, are known to be underestimated. Studies suggest that just one in 10 cases is ever reported. This abominable crime, the legal definition of which has been amended several times, subjects the victim to such a high degree of stress that it leaves deep wounds on the body and mind.

Approximately half of all girls and women who experience sexual violence develop post-traumatic stress disorder (PTSD), a highly debilitating psychiatric disorder that is becoming better understood in this population due to work by researchers at the Federal University of São Paulo (UNIFESP). At the outpatient clinic of the University’s Research and Care Program for Violence and Post-Traumatic Stress (PROVE), a group formed by psychiatrist Marcelo Feijó de Mello investigates the psychological and physiological alterations experienced by those who experience such a harmful event.

“The trauma caused by sexual violence appears to be so intense that it leads to the development of a post-traumatic stress disorder with different characteristics to those observed when the disorder is caused by other events, such as being

robbed at gunpoint,” says psychiatrist Andrea Feijó de Mello, the wife of Marcelo and coordinator of PROVE who headed the clinical trial that evaluated two forms of treatment for participants: antidepressant medication and psychotherapy. One difference is that victims of sexual violence almost always have depression, not as a secondary disorder (comorbidity) but as part of this specific type of PTSD. Another is that they develop a type of long-term mild inflammation that can accelerate ageing, evidenced by wear of the telomeres (structures responsible for making our DNA stable), which is a marker of cell ageing.

Eighty-six women and 31 girls who developed PTSD as a result of rape agreed to participate in the PROVE study, one of the few studies in the world to involve only victims of this form of sexual violence. All participants received medical attention—including medication to prevent pregnancy and HIV—at Pérola Byington Hospital, a renowned women’s health centre in the São Paulo state capital and were later referred to PROVE. There, they twice underwent a series of psychological, blood, genetic, and imaging exams to assess different aspects of their physical and mental health: once shortly after the assault and then again a year after joining the study. Many did not return for the second set of tests because they lived a long distance from the hospital, were scared of leaving the house and being attacked again, or were uncomfortable returning to an environment where they spent so much time talking about the traumatic event. Despite the high dropout rate, the results are helping to identify particular elements of PTSD caused by sexual assault.

Of the 58 participants who agreed to take part in most of the exams and tests, 96.5% had depression, which is usually seen in approximately half of all people with PTSD. Ana Teresa D’Elia, a psychiatry PhD student under the supervision of Andrea Mello, also observed an unusual response in two hormones associated with stress in these women: adrenocorticotropic hormone (ACTH), produced in the brain by the pineal gland, and cortisol, produced by the adrenal glands.

The stress of a real or perceived danger activates a cascade of hormones—including ACTH and cortisol—that increase energy availability and prepare the body for fight or flight. Once the threat has passed, the brain inhibits the production of cortisol. With PTSD, this system malfunctions, and the brain becomes hypersensitive to cortisol, remaining alert even when the hormone levels in the blood are low. However, D’Elia observed the opposite in rape victims: the brain was less sensitive to cortisol. As a result, they had

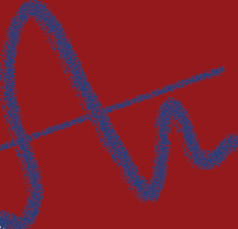
higher cortisol levels, which remained elevated even after a year of treatment with antidepressants, psychotherapy or both, despite greatly alleviated symptoms, according to an article published in *BMC Psychiatry* in 2021. This hormonal imbalance and the high rates of depression reinforce the recent hypothesis of UNIFESP researchers that depression is a typical feature of PTSD caused by sexual violence rather than a separate disease that occurs simultaneously.

In high doses and for long periods, cortisol damages the cells of various organs (including the brain), which then begin to release inflammatory substances. A year after the first tests, D’Elia identified high concentrations of four major inflammation-causing molecules in the blood of rape victims. These levels were higher than those detected in the control group of volunteers who had not experienced sexual trauma and did not have PTSD, the team reports in an article set to be published in the *Journal of Psychiatric Research* in November. Other studies have identified inflammation in the bodies of people with PTSD closer to the time of the traumatic event. “Current research suggests that the immune systems of these women are somehow reprogrammed to respond to aggression,” says Elisa Brietzke, a Brazilian psychiatrist from Queen’s University, Canada, who investigates inflammation in patients with mental illness and was not involved in the study. “This is a sign that sexual trauma can have a long-term—possibly permanent—impact on physical and mental health.”

Persistent inflammation, which is common in certain mental disorders as well as chronic diseases, such as obesity, diabetes, cardiovascular problems, and cancer, appears to accelerate the ageing process. One way to quantify this effect is to

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measure the length of telomeres, the structures at the ends of chromosomes. Telomeres help maintain the stability of genetic material, but they become slightly shorter each time the cell divides. After a certain point, the cell stops multiplying, reducing the tissue's ability to recover.

As part of her PhD under the supervision of Sintia Belangero at UNIFESP, geneticist Carolina Muniz Carvalho evaluated telomere lengths in the blood cells of 64 rape victims with PTSD. They all had shorter telomeres than those in the control group, something already observed in other studies. The difference, however, was only statistically significant among women with a specific symptom: the reliving of traumatic experiences, characterized by the spontaneous recollection of events and frequent nightmares. According to the results of this study, published in *Frontiers in Psychiatry* in May, the difference in telomere length disappeared one year after the traumatic experience, either resulting from treatment or due to the fact that a significant number of women did not return for the second round of tests (only 24 out of 64). "The most plausible hypothesis is that PTSD and its symptoms lead to telomere shortening," explains Belangero, head of the genetic part of the study.

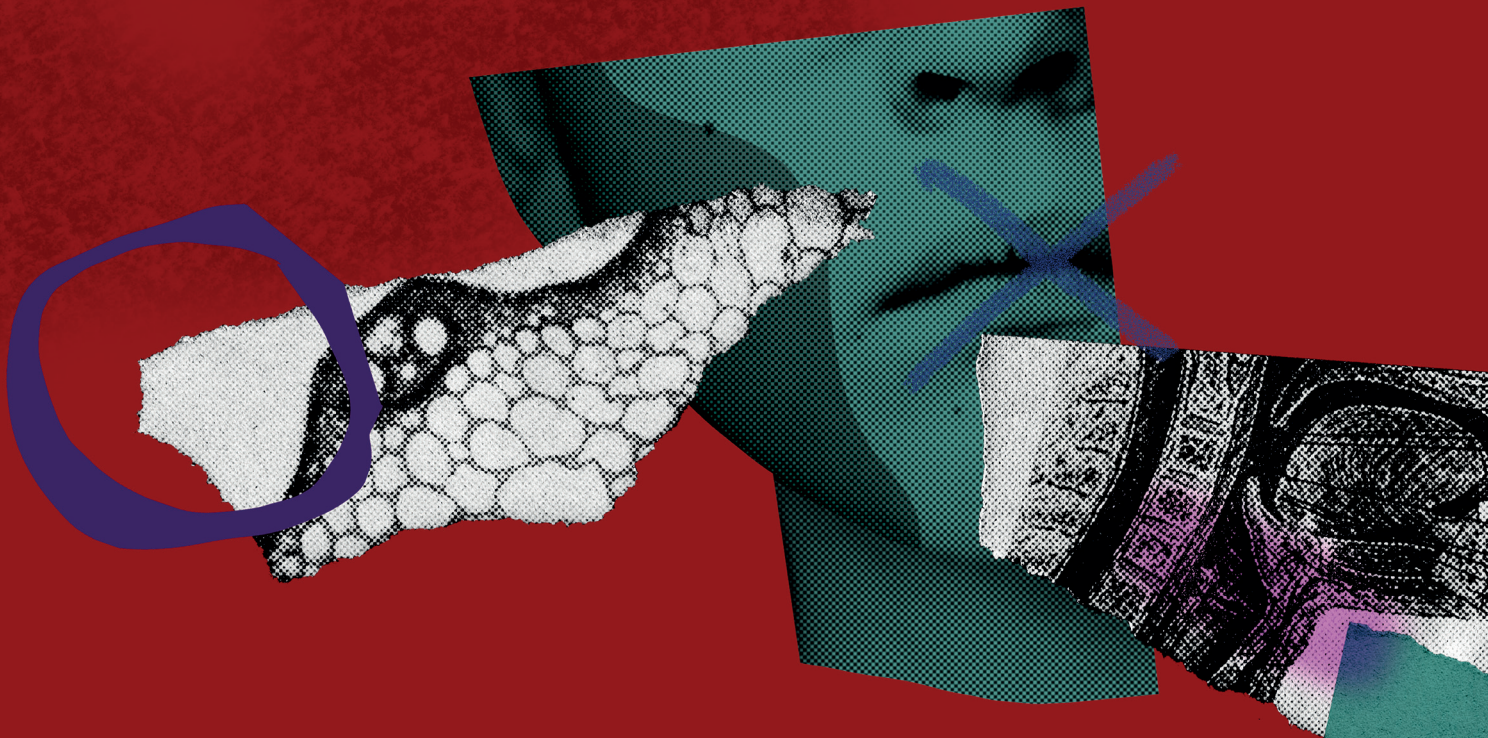
What is now called PTSD first began to be conceived at the end of the nineteenth century—some see similarities in descriptions written by American physician Jacob Mendes da Costa (1833–1900), others in the work of French neurologist and psychologist Pierre Janet (1856–1947). Marked by spontaneous and unwanted memories of the event, recurring nightmares, feelings of guilt and constant vigilance, the disorder causes intense psychological suffering. For much of the most recent

century, PTSD was known as battle neurosis or combat fatigue and associated with the experiences of soldiers.

Mass urbanization and the spread of urban violence brought with it a problem that was previously thought to be exclusive to situations of war. Over time, PTSD started being identified in victims or witnesses of other forms of aggression, such as kidnapping, armed robbery, and domestic violence. In the latest version of the American Psychiatric Association's diagnostic manual (DSM-5), PTSD is no longer classified as an extreme form of anxiety and is now in a category of its own: disorders related to trauma and other stressors, such as sexual violence.

Rape and other forms of sexual assault are among the events that most often lead to PTSD in Brazil. In 2007 and 2008, in the first epidemiological study to measure the frequency of PTSD in two of the largest cities in the country, 3,744 people from various sociocultural and socioeconomic backgrounds were interviewed in São Paulo and Rio de Janeiro. When analysing the data, psychiatrist Mariana Pires da Luz of the Federal University of Rio de Janeiro (UFRJ) found that 44% of rape victims and 49% of women who suffered childhood sexual abuse had symptoms of the disorder. According to the results published in the *Journal of Psychiatric Research* in 2016, this high rate was surpassed only by that of people who had experienced war (68%), although this group is very small in Brazil. "The trauma of being raped appears to be as impactful as experiencing war," says Marcelo Feijó de Mello.





Two common involuntary responses help provide an idea of the intensity of the trauma triggered by sexual violence. Of the women treated at PROVE, 63% said they experienced a change in consciousness during the assault that momentarily removed them from reality. Known as dissociation, this reaction is a known psychological defence mechanism. When faced with the threat of death, the mind enters an almost oneiric state that alters a person's perception of reality, making them feel like they are in a dream or nightmare and sometimes erasing parts of the event from their memory. According to an article published in the *Journal of Interpersonal Violence* in July, women who experienced dissociation later manifested more severe cases of PTSD.

Further analysis of 29 of these women revealed that 72% experienced another response that sometimes occurs in cases of extreme fear: tonic immobility. When seemingly faced with inevitable death, a small region of the brain called the amygdala, responsible for coordinating fear responses, triggers chemical signals that affect other areas of the brain and body, leading to muscle paralysis. "In these situations, the person is awake, but their muscles do not respond, and their body can even present analgesia," says Mauro Mendlowicz, a psychiatrist from Fluminense Federal University (UFF). "No matter how much they want to, they cannot scream or run away," explains the scientist, who is part of a pioneering team that identified tonic immobility in victims of traumatic events in Rio de Janeiro.

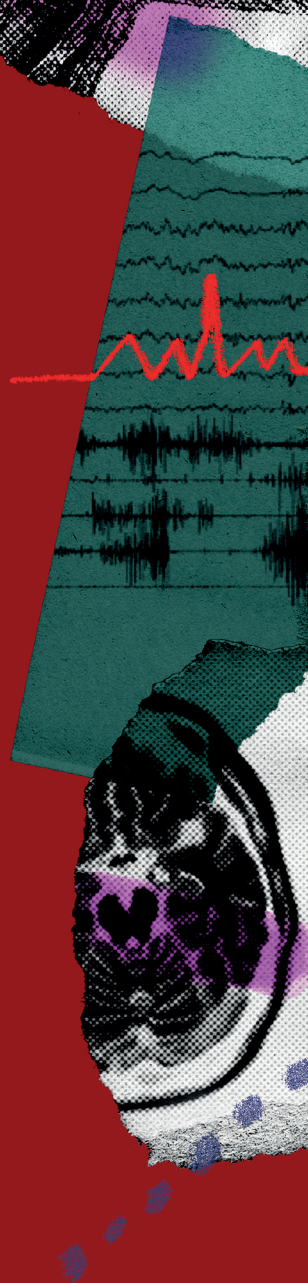
"Women who have these reactions are very poorly understood when they go to police stations and

nonspecialist health services," says Andrea Mello. "The people attending them sometimes mistakenly think that the victim's lack of reaction demonstrates consent, when actually they have no control over these defensive reactions."


Despite being victims, these women often feel guilty and extremely ashamed. As a result, many are reluctant to seek help, report the problem to authorities, or file a complaint against their attackers. "Many of the people we serve live on the peripheries of or in the same communities as their aggressors," highlights PROVE psychiatrist Mary Yeh. "In many cases, abusers return to harass their victims and sometimes threaten them after being reported," she says. Some victims are treated with suspicion by those who are supposed to help them. This was the case for one teenager raped at gunpoint and abandoned in a bush, for example. She was left naked and searching for help, and initially, neither the police nor her own family believed her when she told them what had happened.

The participants of the study generally had greater difficulties with comprehension, reasoning, and attention than the control group of women and girls in the same age range who had not suffered this type of violence, according to an analysis by neuropsychologists Adriana Mozzambani, Nathalia Emygdio, Fernanda Rodrigues Gomes, and Tania Camargo. The difference was greater among women who also had sleep problems, Camargo noted. "There is a suspicion that women with worse cognitive performance assess risk situations less efficiently and become more vulnerable," says Gomes.

Neuroscientist Andrea Jackowski and psychiatrist Ana Carolina Milani captured brain images



THE TRAUMA OF BEING RAPED APPEARS TO HAVE AS MUCH OF AN IMPACT AS EXPERIENCING WAR



of girls with PTSD while they performed certain activities and noticed disorganization in the default mode network—a group of interacting brain regions active when a person is thinking inwardly, self-reflecting, and remembering important life events. The problem appears to result from reduced connectivity between the cells of the hippocampus, a brain region linked to memory acquisition. In an article published in *Neurobiology of Stress* earlier in 2022, the researchers described how the symptoms of the disorder decreased and this brain network returned to normal function after psychotherapy sessions, sometimes together with the use of antidepressants. “After six months of treatment, we were able to help these girls resume an almost normal life,” says Milani.

“We need to think of strategies that work on a large scale in the public health system,” stresses Jackowski. One strategy could be the adoption of interpersonal therapy, a form of psychotherapy intended to help patients reestablish bonds with friends and family that can be applied in a group setting. A clinical study of 74 women revealed that interpersonal therapy was as effective for reducing PTSD symptoms as the antidepressant sertraline, which is commonly used to treat PTSD.

The results obtained to date by the UNIFESP group highlight another factor that is just as important as treatment for psychological suffering: good sleep. At the beginning of the study, the 74 participants completed questionnaires about anxiety, depression, and sleep disorders to provide a clinical overview of the quality of their sleep. At both the first assessment and a year later, they were invited to spend a night at UNIFESP’s Sleep

Institute to undergo polysomnography, an exam that records electrical brain activity and heart-beat and breathing data during sleep. All of the participants met the clinical criteria for at least one sleep disorder, from insomnia to nightmares about the event, according to a study published in the *European Journal of Psychotraumatology* in 2021. Clinical data showed that they had more severe insomnia and poorer sleep quality than women in the control group, although the polysomnographies did not identify any differences in the sleep patterns of the two groups.

After treatment with psychotherapy and medication, patients who continued to sleep poorly continued to experience more PTSD symptoms. “Sleep-focused treatment not only improves sleep but also PTSD symptoms,” says Yeh, coauthor of the article. Other research into PTSD has indicated that the more symptoms a person has, the worse they sleep; additionally, poor sleep quality can increase a person’s chance of developing the disorder. “Both problems need to be treated because one influences the other,” explains neurologist Dalva Poyares, coordinator of the sleep phase of the project.

Studies that follow a greater number of participants for longer periods of time are needed to corroborate the effects observed by the PROVE team and to confirm that persistent inflammation leads to premature cellular ageing in this population. More effective interventions could be identified that could be administered earlier to prevent problems from progressing. “We need to better understand some of these phenomena,” says Marcelo Feijó de Mello. “From a health care standpoint, we need to improve the way the health system and public security agencies attend to these victims and increase the number of specialist services available.”

While you read this text, another woman or girl was raped in Brazil. ■

Project

Post-traumatic stress disorder and neuroprogression: New approaches to understanding the effect of violence on mental function (no. 14/12559-5); Grant Mechanism Thematic Project; Principal Investigator Marcelo Feijó de Mello (UNIFESP); Investment R\$2,967,600.56.

Scientific articles

D’ELIA, A. T. *et al.* Increased immuno-inflammatory mediators in women with post-traumatic stress disorder after sexual assault: 1-year follow-up. *Journal of Psychiatric Research*. Vol. 15, pp. 241–51. Nov. 2022.

CARVALHO, C. M. *et al.* Shorter telomeres related to posttraumatic stress disorder re-experiencing symptoms in sexually assaulted civilian women. *Frontiers in Psychiatry*. May 19, 2022.

Other scientific articles consulted for this report are listed in the online version.