Using drugs to weaken traumatic memories

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A potential new approach to treat posttraumatic stress disorder: After taking the antibiotic doxycycline, study participants remembered an unpleasant event considerably less, as experiments conducted by a team of researchers from the University Psychiatric Hospital and the University of Zurich reveal.

Physical violence, war or a natural disaster can trigger posttraumatic stress disorder (PTSD). Those affected keep reliving the traumatic event—through memories that hit them out of the blue or as recurring nightmares. As this psychological wound can't always be treated successfully with psychotherapy, scientists have long been looking for a way to influence trauma memory using drugs. So far, possibilities tested in animal models have not been suitable or effective enough for this purpose. Now, however, researchers from the University Psychiatric Hospital and the University of Zurich have successfully tested a new drug that considerably weakens the recollection of a negative experience in humans.

Doxycycline inhibits enzyme involved in memory formation

The team headed by Dominik Bach, an UZH professor and a physician at the University Psychiatric Hospital, presents a new approach. They studied how inhibiting an enzyme that is important for strengthening connections between nerve cells affects traumatic memories. Lab experiments only recently revealed that proteins from the extracellular matrix, the space between nerve cells, are necessary for memory

formation. Known as metalloproteinases, these enzymes are found throughout the body and involved in the development of heart disease and various cancer strains. The antibiotic doxycycline inhibits the activity of these enzymes and has already been tested for several of these diseases. Now the UZH professor and his two study authors examined how doxycycline affects memory formation.

Negative reactions two thirds weaker

Almost 80 people divided into an experimental and a control group took part in the study. Test subjects were given mildly painful electrical impulses, which they learned to associate with a specific color. The experimental group received 200 mg of doxycycline beforehand, the control group a placebo. The test subjects in the control group showed increased startle responses upon seeing the color when tested seven days later. "For those in the experimental group, the later startle responses were around two thirds weaker than in the control group," explains Bach. "Therefore, we demonstrate for the first time that doxycycline diminishes emotional memory if taken before a negative event."

Usable in combination with psychotherapy

The results show that metalloproteinases are not just useful tools in the lab; they are also relevant for memory formation in humans. According to Bach, these enzymes provide key starting points for the development of therapeutically effective substances. "Based on what we know today, though, doxycycline could probably already be used to dampen existing emotional memories—if patients so desire," says the doctor from the Department of Psychiatry, Psychotherapy and Psychosomatics. This treatment would involve specifically activating existing traumatic memories and weakening them by administering doxycycline. "We're planning to test this combined therapy model first in healthy people and

then in the clinic," concludes Bach.

More information: Dominik R. Bach, Athina Tzovara, Johanna Vunder. Blocking human fear memory with the matrix metalloproteinase inhibitor doxycycline. *Molecular Psychiatry*, April 4, 2017. DOI: 10.1038/ MP.2017.65

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