Vaccine hope for post-traumatic stress

Development of anxiety and fear alleviated by manipulating immune system in rodents.

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Traumatic experiences, such as those encountered during warfare, can cause long-lasting stress.

Tweaking the immune system could be key to treating, or even preventing, post-traumatic stress disorder (PTSD). Research in rodents suggests that immunizing animals can lessen fear if they are later exposed to stress.

Researchers have known for some time that depression and immune-system health are linked and can affect each other. Early clinical trials have shown that anti-inflammatory drugs can reduce symptoms of depression[1], raising hopes that such treatments might be useful in other types of mental illness, such as PTSD.

"I think there's kind of a frenzy about inflammation in psychiatry right now," says Christopher Lowry, a neuroscientist at the University of Colorado Boulder. He presented results of experiments probing the link between fearful behaviour and immune response at a meeting in Victoria, Canada, last week of the International Behavioral Neuroscience Society.

Studies of military personnel suggest that immune function can influence the development of PTSD. Soldiers whose blood contains high levels of the inflammatory protein CRP before they are deployed[2], or who have a genetic mutation that makes CRP more active[3], are more likely to develop the disorder.

To directly test whether altering the immune system affects fear and anxiety, Lowry and colleagues injected mice with a common bacterium, *Mycobacterium vaccae,* three times over three weeks to modulate their immune systems. The scientists then placed these mice, and a control group of unimmunized mice, in cages with larger, more aggressive animals.

Mice that had received the injections were more 'proactive' in dealing with the aggressor, Lowry says, rather than simply surrendering, as most mice do. And the guts of the immunized mice remained healthy, whereas the animals in the control group developed inflamed colons and their gut bacteria shifted to favour species associated with stress.

Stress relief

In a second experiment, Lowry and colleagues injected rats with *M. vaccae* and conditioned them to fear a sound that was associated with an electric shock to the foot. This fear was then 'extinguished' by exposing the animals to the sound without the foot shock.

Immunized rats lost their fear much more quickly than unimmunized animals, suggesting that immunomodulation could be a treatment for PTSD as well as a preventive measure.

Lowry says that his group is considering clinical trials of the therapy. Because *M. vaccae* has been extensively used in humans as a treatment for other diseases, he hopes that regulators will approve the trial plans fairly quickly.

Jessica Gill, who studies neurogenomics at the US National Institute of Nursing Research in Bethesda, Maryland, says that the idea of preventive treatment for PTSD is interesting. “It definitely is conceivable something like this could be translated to use in populations where we know they’re going to be under stress,” she says.

In a separate study also presented at the neuroscience meeting, researchers taught mice to fear a sound by delivering an electric shock each time it played. The team, led by neuroscientist Matthew Young of the Yerkes National Primate Research Center in Atlanta, Georgia, then injected the animals with molecules from the surface of bacteria to trigger an immune response.

Twelve hours later, the scientists tested the animals’ reaction to the sound, and found that mice that had been injected acted in a more fearful way than did mice in a control group.

“It’s massively intriguing,” says Bill Deakin, a neuroscientist at the University of Manchester, UK. He is beginning a clinical trial to give 200 people with schizophrenia the antibiotic minocycline, which blocks inflammation in the brain, to determine whether this treatment lessens the shrinkage in the brain's grey matter that is seen early in the disease. A smaller study found that this treatment lessened symptoms of the disease [4].

Deakin hopes that treating people at genetic risk of schizophrenia or who are showing early signs of psychosis could lessen the disease’s symptoms once it develops. “We have all these little clues,” he says.

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