# Social Stress Boosts Immune System's Flu-Fighting Abilities

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A new study in mice suggests that, in certain cases, stress may enhance the body's ability to fight the flu.
Short bouts of intense social stress improved the ability in the mice to recover from the flu. The stress apparently did so by substantially boosting the production of specialized immune cells that fought the virus.
"Stressed mice had a stronger immune response and were able to fight off the infection faster," said Jacqueline Wiesehan, a study co-author and a graduate fellow in oral biology at Ohio State University.

These special immune cells are called T cells and are part of the immune system's memory response. T cells "remember" specific infectious agents and can launch future attacks against these intruders.

The researchers hope to learn more about the mechanisms behind the memory response, and to use this information to develop more effective flu vaccines in the future, said David Padgett, a study co-author and an associate professor of oral biology at Ohio State.

Wiesehan, Padgett and John Sheridan, the study's lead author and a professor of oral biology at Ohio State, presented their findings on April 3 at the Experimental Biology 2005 conference in San Diego. The three also worked on this study with Michael Bailey, a postdoctoral fellow in oral biology at Ohio State.

The immune system develops a memory response to the flu vaccine

because the vaccine contains inactivated viral particles. The body responds by producing antibodies, special proteins that fight intruders, or antigens, such as bacteria and viruses. Sometimes, people who get the vaccine feel as if they actually have a mild case of the flu. They actually don't, Padgett said. Rather, those flu-like symptoms are just the body's response to making antibodies to the antigen.

New flu vaccines are created every year, and, according to the World Health Organization, are about 70 to 90 percent effective in preventing influenza.

"Right now, we try to vaccinate a large percentage of our elderly population in hopes of protecting most people from influenza," Padgett said. "But older adults may not get the same level of protection from the vaccine as younger adults would. We think that the memory response may be considerably different in older adults, whose immune systems generally don't work as well as a younger person's."

At the beginning of the study, some of the mice were caged in groups of three. One aggressive mouse, meant to disrupt the social environment in the cage, was put in each of thee cages for two hours at a time for six consecutive days.

At the end of the last stress session, the researchers infected both the subordinate mice that had endured stress and those mice that weren't caged with an aggressive mouse with a strain of influenza virus that can also infect humans. The mice were infected through their noses. This was the first time that the animals' immune systems had been exposed to the virus, and the researchers wanted to see what effect the stress would have on the immune system's memory response.

Three months later, the researchers injected either a small amount of saline solution or influenza virus into the footpad of one hind paw of

each mouse. This kind of viral challenge caused what scientists call a "delayed-type hypersensitivity" response; the skin test routinely used to test a person for tuberculosis also causes this kind of response.

"It takes about a month for the body to develop a strong pool of memory T cells that are ready to fight another virus," Wiesehan said. "We waited a little longer to make sure this memory response was in place."

The influenza challenge caused the infected paws to redden and swell. The researchers measured the thickness of paws daily until the swelling went down – this measurement gave the researchers an idea of the number of cells responding to the viral antigen.

The affected paws of the stressed mice were noticeably more swollen than those of the non-stressed mice, suggesting that the immune system's of the stressed mice had had produced more immune cells that could respond to this strain of flu virus.

Three weeks later, the mice were re-infected with influenza virus through the nose. About a week later, the researchers examined the spleens and lungs from all of the mice. (Immune cells, including T cells, are activated in the spleen and lymph nodes, and then move to the lung cells where the flu virus has infected lung cells.)

The researchers measured the levels of flu-specific T cells in both organs, and found a greater number of the cells in both the spleens and lungs of the stressed mice.

While the mice in the study were re-infected with the identical strain of flu, there's a good chance that a person would not catch the same strain again, since flu viruses continually mutate.

Still, the T cells created during the initial infection can often respond to

and attack variations of the same virus, Padgett said.

"Memory to a specific virus is considered life long, but the chance that someone will be re-infected with the same virus declines with time," he said. "Yet the antibodies that develop with the first illness can often recognize other, related strains."

The researchers now hope to figure out how the stressors affect memory response functions in people, particularly the elderly.

"If we can gain a solid understanding of how vaccines affect individual memory responses, we may be able to develop vaccines that elderly people could respond better to," Padgett said.

Curiously, similar work by Padgett, Sheridan and their Ohio State colleagues has shown that social stress can reactivate a latent herpes simplex virus type I in mice. HSV-1 causes cold sores around the mouth, and lesions on the face and genitals in humans.

"Social stress isn't necessarily a great thing," Padgett said. "But there must be some kind of adaptive advantage for this response – it seems to benefit the body by enhancing immune memory in some way.

"There may be some hormonal changes that actually promote the development of the memory T cells that are important in fighting of influenza," he continued. "The goal is to ultimately figure out what those changes are."

Source: Ohio State University