Moments of acute stress can cause molecular alterations in immune response

March 1 2016

Chronic psychosocial and emotional stress has well-documented negative effects upon the human immune system, measurably increasing the risk of disease. Much less is known about the health effects of acute but transitory episodes of stress, such as jumping out of an airplane. Do these panic-inducing moments also raise the risk of stress-related conditions and disorders, such as cardiovascular disease, sleep dysfunction, impaired wound healing, depression and obesity?

A team of researchers at University of California, San Diego School of Medicine, Stony Brook University in New York and elsewhere addressed that question by asking study participants to literally jump out of a plane, taking blood samples before and after to measure key immune response indicators.

Their findings are published in the March 4 issue of *Brain, Behavior and Immunity*.

"In our everyday lives, acute stress is manageable and does not cause physiological damage," said study co-author Brinda Rana, PhD, associate professor in the Department of Psychiatry at UC San Diego School of Medicine. "However, for those who experience it frequently, it can be a risk for chronic diseases and disorders, such as cardiovascular and immune modulated inflammation. And since the health of the immune system is crucial to protection against pathogens and other diseases, it's important to understand the impact of stressful life events on the ability of our immune system to properly do its job."

The study involved 39 individuals (24 males, 15 females) who had independently contacted a New York-area skydiving school to schedule a first-time tandem sky dive in which the student skydiver was connected by harness to an instructor who guided the student through the jump, freefall and landing.

All of the participants were healthy adults with no history of cardiac or mental illness. They were divided into two groups: 13 would have their RNA expression profiles measured to understand molecular signatures associated with stress, and 26 would be studied by flow cytometry to access changes in immune cell composition in blood.

Blood sampling was precisely scheduled by the lab of co-author Lilianne R. Mujica-Parodi, PhD, associate professor in the Department of Biomedical Engineering at Stony Brook University. Participants provided a baseline blood sample at 9:15 a.m. within one week prior to or one day after the sky dive. On the day of the skydive, all participants awoke at 6:30 a.m. and arrived at Stony Brook University Hospital at 7:30 a.m. where "pre-boarding" samples were collected at 9:15 a.m., one hour before take-off.

The actual jump occurred at 10:30 a.m., when the airplane reached an altitude of 11,550 feet. Skydivers landed five minutes later, with post-landing samples taken at 10:45 a.m. and again at 11:30 a.m. back at the hospital.

"Our tandem skydive instructor is also a phlebotomist," said Mujica-Parodi. "He carried the blood draw supplies with him on the jump and was poised to draw blood as soon as the skydivers hit the ground."

In addition, saliva samples were collected every 15 minutes from 9:15 a.m. to 11:30 a.m. on both the day of the sky dive and the baseline hospital day.

Previous research has shown that acute, short-term stress provokes a mixed bag of immune responses, some beneficial, some not. For example, numbers of natural killer cells, which are part of the innate immune response, increase, but skin healing capacity is reduced. The novelty of the study, said Rana, is leveraging advanced computational and molecular tools to assess large-scale immune system responses, to more finely detail the effects of acute, short-term stress.

"Our study is the first to probe the rapid transcriptomic (messenger RNA) changes in white blood cells that occur before and after an acute psychological stressor," said Rana. "We identified specific genes and pathways involved in both the innate and the adaptive immune response that were dysregulated in response to the acute stress of the sky dive, and which returned rapidly to natural baseline levels one hour after the jump."

Interestingly, the researchers noted that modules of coordinately expressed genes responding to stress were different between male and female skydivers, which they say may help explain gender differences observed in development of stress related cardiovascular and autoimmune disorders, as well as conditions like post-traumatic stress disorder (which is twice as common in women).

Nadejda Beliakova-Bethell, PhD, first co-author of the study and an assistant project scientist at UC San Diego, with background in infectious diseases, said while the research was exploratory, it laid the foundation for future, more detailed experiments to elucidate the contribution of stressful life events and exposure to pathogens to the functioning of the immune system.

"The immune response to stress is similar to the response to pathogens," said Beliakova-Bethell. "An instance of an acute stress or infection activates the immune system, while chronic stress or infection results in

the exhaustion of the immune system, making it less effective at responding to new stressful events or new pathogens. The effects on the transcriptome of white blood cells, observed in this study, were very transient, returning to baseline levels within one hour after landing, but with repeated acute or chronic stress, these transcriptomic changes would be expected to be more permanent, and may be similar, at least in part, to the effects of chronic viral infection.

"Future studies could make an important contribution to identifying gene targets for developing therapeutic strategies that would help people to cope with the prolonged effects of a stressor or to fight new infections. This would be specifically important for the elderly, who would have accumulated effects of stressors and infections throughout their lifetimes."

More information: Michael S. Breen et al. Acute psychological stress induces short-term variable immune response, *Brain, Behavior, and Immunity* (2015). DOI: 10.1016/j.bbi.2015.10.008

Provided by University of California - San Diego